

A Collection of

NIDA NOTES

NATIONAL INSTITUTE
ON DRUG ABUSE

Articles That Address



DRUG
ABUSE
TREATMENT

U.S. Department of Health and Human Services
National Institutes of Health
National Institute on Drug Abuse

NN0026

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Introduction

The National Institute on Drug Abuse (NIDA) supports most of the world's research on drug abuse and addiction. NIDA-funded research enables scientists to apply the most advanced techniques available to the study of every aspect of drug abuse, including:

- genetic and social determinants of vulnerability and response to drugs;
- short- and long-term effects of drugs on the brain, including addiction;
- other health and social impacts of drug abuse, including infectious diseases and economic costs;
- development and testing of medications and behavioral treatments for abuse and addiction; and
- development and evaluation of effective messages to deter young people, in particular, from abusing drugs.

Included in this document are selections of topic-specific articles reprinted from NIDA's research newsletter, *NIDA NOTES*. Six times per year, *NIDA NOTES* reports on important highlights from NIDA-sponsored research, in a format that specialists and lay readers alike can read and put to use. Selections like the current one are intended to remind regular *NIDA NOTES* readers and inform other readers of important research discoveries during the periods they cover.

We hope the information contained here answers your needs and interests. To subscribe to *NIDA NOTES* and for further information on NIDA's drug abuse and addiction research, please visit our Web site at www.drugabuse.gov.

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Court Mandates Help Men With Antisocial Personality Disorders Stay in Treatment

Men with co-occurring substance abuse and antisocial personality disorders may particularly benefit from judicially mandated addiction treatment. Such legal pressure has been shown to exert a positive effect on treatment retention in a general population of drug abusers (see What the Numbers Say).

Dr. Stacey B. Daughters and colleagues at the University of Maryland recently studied 236 men who began therapy for substance abuse problems. Ninety-three of the men met standard criteria for antisocial personality disorder (ASPD), a condition characterized by chronic behavior problems, deceitfulness, and lack of conscience and regard for others.

Among men without ASPD, 85 percent remained in therapy whether the treatment was voluntary or mandated. However, the investigators found that among men with ASPD, about 94 percent of those who were legally required to participate in residential substance abuse treatment remained for a month, compared with just 63 percent of those who had volunteered to enter treatment.

Although ASPD is rare in the general population, researchers estimate that 40 to 50 percent of people



in drug treatment programs have the disorder. Moreover, prior research suggests that ASPD increases the risk for a addiction treatment drop-out, relapse, and, among those with jail sentences, a return to criminal behavior.

The Maryland team's findings have two important implications for substance

abusers with ASPD: Judicial mandates offer a way to keep them in addiction treatment programs, and voluntary participants may require special interventions to keep them actively engaged in therapy.

Source

- *Journal of Substance Abuse Treatment* 34(2):157-164, 2008. **NN**

Research Addresses Needs of Criminal Justice Staff and Offenders

By Lori Whitten, *NIDA NOTES* Staff

NIDA established the Criminal Justice-Drug Abuse Treatment Studies (CJ-DATS) project in 2002 to reduce substance abuse and recidivism among offenders following their release from jail or prison. CJ-DATS investigators in nine research centers collaborate with criminal justice partners to fashion and test science-based, practical tools for integrating drug abuse treatment in the Nation's prisons and probation and parole programs.

Dr. Bennett Fletcher serves as CJ-DATS program scientist and provides NIDA input to the network's planning and decisionmaking. According to Dr. Fletcher, "As many as half of the individuals serving sentences in the Nation's jails and prisons have drug problems. The transition from detention or incarceration is a period of high risk for relapse to drug use, acquisition and transmission of infectious diseases, and drug-related recidivism. In its first 5 years, CJ-DATS identified a range of effective practices to reduce these risks. The project is now beginning a new phase of research to determine how correctional and community agencies can most efficiently and effectively implement and sustain these practices."

Identifying Effective Practices

The first phase of CJ-DATS encompassed 13 studies in three areas:

Brief Screening and Assessment Instruments—These studies give criminal justice staff user-friendly tools to identify an offender's need for treatment and criminal justice services and to monitor his or her treatment progress. The researchers have designed a variety of instruments to help providers determine whether a prisoner is responding to therapy, requires referral to a mental health provider, or will need intensive treatment after release. Studies show that these instruments have good reliability, validity, sensitivity, and specificity.

Strategies to Promote Successful Community

Re-entry—Many individuals need help to stay engaged in addiction treatment as they re-enter communities fol-

Effective Treatment Is Not Widely Available

Less than 10 percent of adults and about 20 percent of adolescents with substance abuse problems in the Nation's jails, prisons, and probation programs can receive treatment on a given day, according to the National Criminal Justice Treatment Practices Survey (NCJTPS). Although 65 percent of adult facilities report that they offer substance abuse treatment, the number of people who can participate in these programs is often severely limited.

These findings further reveal the scope of the problem highlighted by previous research indicating that the most frequently provided services for adults and adolescents—substance abuse education and low-intensity group therapy (less than 4 hours a week)—are not likely to help offenders change their behavior. The survey also disclosed that only 40 percent of adult facilities and 29 percent of juvenile facilities reported having full-time personnel to provide drug abuse therapy. For more information, see the *Journal of Substance Abuse* 32 (3), April 2007; this special issue of the journal was dedicated to NCJTPS.

lowing release from prison. Many also require assistance with housing, employment, family relationships, health issues, and building a social support network. CJ-DATS researchers and their criminal justice partners together developed interventions (see box) to reduce re-entering adults' and adolescents' criminal activity, substance abuse relapse, and sexual behaviors that carry high risk of HIV/AIDS and other sexually transmitted diseases. Investigators have now tested interventions in seven randomized controlled trials, with 3- and 9-month followups. Several appear promising.

Surveys of Treatment Services for Offenders—A team led by the CJ-DATS Research Center at Virginia Commonwealth University and the University of Maryland conducted a National Criminal Justice Treatment Practices Survey to inventory treatments available in correctional facilities, community supervision programs, and drug treatment programs with offender clientele. The data included information on treatment providers, frequency and duration of treatment, and the number of offender clients. The results indicate that there is a significant shortage of treatment opportunities for this population (see box).

Another survey, by investigators at the National Development and Research Institutes Rocky Mountain

Research Center, focuses on services for offenders who have both substance abuse and other mental disorders—a large and growing percentage of the U.S. criminal justice population. This survey is using the specially developed CJ-DATS Co-occurring Disorders Screening Instrument (CODSI) to identify patients with dual disorders. The findings will provide a foundation for efforts to improve treatment services for these offenders.

In a third practice-monitoring project, CJ-DATS investigators are developing a Web-based system to inventory drug court processes and treatment services for the drug court participants. The researchers have pilot-tested a drug court management information system based on the Center for Substance Abuse Treatment's Web Infrastructure for Treatment Services (WITS) system.

New Directions

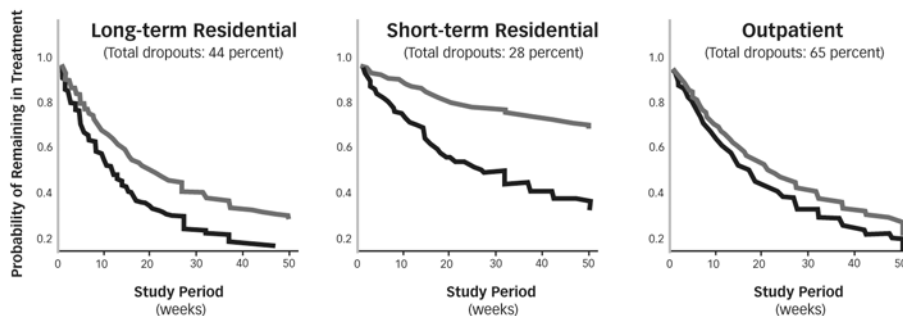
Over the next 5 years, CJ-DATS investigators will shift their focus to issues of implementation. NIDA program officer Dr. Akiva Liberman says, "The new studies will identify efficient and effective ways to implement screening and assessment tools, a continuum of HIV care, and behavioral or medications interventions. They will provide criminal justice organizations with science-based information on how staffing, infrastructure, policies, practices, and incentive systems may be adjusted to facilitate new evidence-based practices." Dr. Liberman will monitor these studies. Dr. Redonna K. Chandler, chief of NIDA's Services Research Branch in the Division of Epidemiology, Services and Prevention Research, says, "Federal, state, and community criminal justice facilities are overwhelmed by the number of offenders with drug problems, and many administrators and staff want to incorporate addiction treatment into their programs. CJ-DATS will offer them evidence-based therapies and information to guide decisionmakers as they integrate treatment into their services."

RESEARCH NETWORK TESTS INTERVENTIONS TO PROMOTE SUCCESSFUL COMMUNITY RE-ENTRY		
Investigators in the Criminal Justice–Drug Abuse Treatment Studies project are comparing standard supervised release from prison with approaches that integrate drug abuse treatment.		
Study	Treatment	Lead Center
Targeted Interventions for Corrections	Six brief, flexible interventions address problems faced by adult offenders re-entering the community: motivation to change behavior, anger management, healthier thinking patterns, communication in relationships, social support, and skills and knowledge to reduce risk of sexually transmitted infections.	Southwest Research Center, Texas Christian University
Step'n Out	In this approach, criminal justice staff monitor specific behaviors (e.g., abstinence, employment searches, and counseling attendance) and reward clients who meet agreed-upon goals with social acknowledgement (e.g., congratulatory letter from parole supervisor) and small material incentives (e.g., partial payment for clothes for job interviews).	Rhode Island Research Center, Brown University and Lifespan Hospitals
Two Re-entry Strategies for Drug-Abusing Juvenile Offenders	Juvenile probation officers trained in cognitive restructuring intervene to change adolescents' belief structures underlying criminal activity and drug abuse. This intervention yielded good results for adult offenders but has not previously been tested in adolescents.	Midwest Research Center, National Development and Research Institutes
Facilitating Adolescent Offenders' Reintegration From Juvenile Detention to Community Life	Multidimensional Family Therapy—an evidence-based treatment for adolescent substance abuse—blends individual and family therapy. The intervention also includes family-based HIV/STI prevention. The results of this component of the study may have implications for adolescent substance abuse treatment beyond the criminal justice system.	Florida Research Center, University of Miami
Transitional Case Management	This team case management intervention focuses on adult offenders' post-release goals, social support, accomplishments, and skills.	Pacific Coast Research Center, University of California, Los Angeles
Restructuring Risky Relationships–HIV	This intervention helps women change problematic thinking patterns about relationships and reduce their HIV risk.	Central States Research Center, University of Kentucky
HIV/Hepatitis C Prevention for Drug-Involved Offenders During Re-entry	This study compared three interventions for men and women: (1) education only; (2) state-of-the-art HIV prevention; and (3) a peer-based, interactive multimedia intervention tailored for gender and ethnicity.	Mid-Atlantic Research Center, University of Delaware

To date, reports of CJ-DATS research have appeared in several publications and in five special issues: *The Prison Journal*, March 2007; *the Journal of Substance Abuse Treatment*, April 2007; *Criminal Justice and Behavior*, September 2007; *Behavioral Sciences and the Law*, July/August 2008, and the *Journal of Psychoactive Drugs*, December 2008. For more information about ongoing research from the CJ-DATS treatment studies, visit www.cjdat.org. **NN**

Legal Pressure Increase Treatment Retention

WHAT THE NUMBERS SAY



SOURCE: Analyses of data collected during the National Treatment Improvement Evaluation Study, which involved publicly funded, nonmethadone treatment programs including long-term residential ($n = 757$), short-term residential ($n = 756$), and outpatient treatment ($n = 1,181$) reported in: Perron, B.E. and Bright, C.L. The influence of legal coercion on dropout from substance abuse treatment: Results from a national survey. *Drug and Alcohol Dependence* 92(1-3):123-131, 2008.

People who participated in substance abuse treatment on the recommendation or requirement of an attorney or criminal justice professional (gray lines) were more likely to stay in treatment than were people who voluntarily chose to participate in treatment (black lines). Legal pressure had the largest effect on treatment retention rates among persons in short-term residential programs, where participants sometimes stayed much longer than the typical 2-month period.

High-Risk Drug Offenders Do Better With Close Judicial Supervision

Low-risk offenders do equally well with and without regularly scheduled court appearances.

By *NIDA NOTES* Staff

Adjusting the frequency of mandatory drug court monitoring sessions according to offenders' risk of lapsing into criminal activity, including drug abuse, can enhance program success rates while conserving resources, according to a recent NIDA-supported study. Researchers found that high-risk drug offenders—those with antisocial personality disorder or prior histories of drug abuse treatment—achieved better outcomes when ordered to attend a judicial status hearing every 2 weeks, rather than at the 4- to 6-week intervals that drug courts typically impose. In contrast, lower risk offenders' treatment success was not compromised when courts required them to appear only if they committed serious or repeated infractions of program rules.

"Our research represents a first step in tailoring adaptive supervision interventions to drug-abusing offenders," says Dr. Douglas Marlowe of the Treatment Research Institute and the University of Pennsylvania, Philadelphia. Dr. Marlowe, Dr. David Festinger, and colleagues conducted the study as part of a broader effort to improve the efficacy and cost-effectiveness of drug court interventions by identifying which components of the model work best for various groups of drug offenders.

Custom Tailoring Court Supervision

Drug courts are intensive, community-based programs that substitute judicially supervised treatment and case management for prosecution or incarceration. Defendants who complete the drug court program and remain arrest-free for 6 months after graduation have their charges dropped and their arrest records expunged. The judicial status hearing, during which a judge rewards achievements and punishes infractions with sanctions that progressively increase in severity, is among the costliest components of drug court programs.

Drs. Marlowe and Festinger designed their study to answer two questions: Would high-risk drug offenders benefit from hearings held more frequently than usual, and would low-risk drug offenders still experience treatment gains if their hearings were held less often than the norm? The researchers had reason to predict the answers would be "yes" to both questions because of observations they had made in a previous study. That study's design and small participant population, however, had not allowed definitive findings on these issues.

MORE-FREQUENT COURT APPEARANCES IMPROVE OUTCOMES FOR HIGH-RISK OFFENDERS

	HIGH RISK*		LOW RISK	
	Biweekly Schedule	Standard Schedule	Standard Schedule	As Needed**
Rate of Graduation from Treatment Program	75%	56%	75%	72%
Average Days of Drug Use in Past 30 Days	8.00	9.51	3.50	4.32
Average Days of Alcohol Intoxication in Past 30 Days	1.40	2.67	2.02	1.30

Graduation rate assessed 12 months after beginning of treatment program; other data collected at 6-month followup.

*Participants were considered high-risk if they had antisocial personality disorder or previous treatment for drug addiction.

**Only scheduled to address serious or repeated infractions of treatment rules.

Participants in the new study were recruited from a misdemeanor drug court in Wilmington, Delaware. Among the drugs that they reported abusing at the time of their assignment to drug court, cannabis was the most common, followed by alcohol, stimulants or cocaine, opiates, sedatives, and hallucinogens. Each participant was assigned to a clinical case manager who coordinated treatment referrals, submitted monthly reports to the judge, and appeared at the participant's judicial status hearings.

Ninety-two of the 279 participants were classified as high-risk because they had an antisocial personality disorder or had relapsed after previous treatment for drug abuse. Within the high-risk group, 42 were assigned to report to drug court biweekly, and 50 reported every 4 to 6 weeks. In the low-risk group, 92 were put on the 4- to 6-week schedule, and 95 were told to appear in court only after serious rule infringements—most commonly failure to attend counseling appointments or provide drug-free urine specimens.

Within a year, 75 percent of the high-risk participants who attended hearings every 2 weeks graduated from the program, compared with 56 percent of high-risk participants assigned to follow the standard schedule. The former

group also provided more drug-free urine samples and reported less alcohol intoxication (see table), as well as less criminal activity.

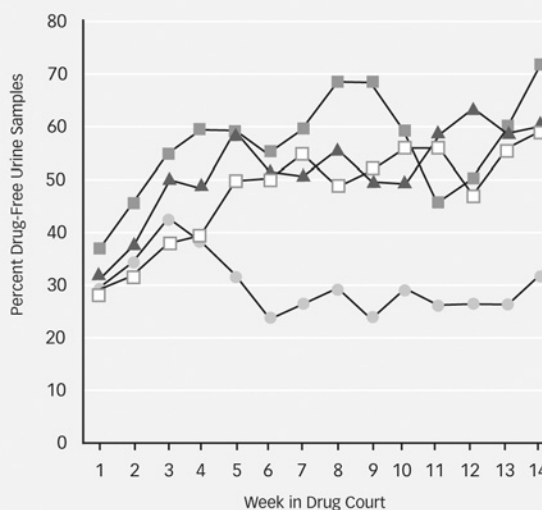
Among the low-risk participants, outcomes were similar regardless of how often hearings took place. For example, program graduation rates were 75 percent among the offenders who appeared in drug court every 4 to 6 weeks and 72 percent among those who appeared in court only when a problem arose, averaging less than two hearings during the study year. “Reducing the number of court hearings for these individuals could permit a program to conserve costly resources without sacrificing client outcomes or public safety,” Dr. Marlowe says.

Room for Improvement

“Adjusting the frequency of court hearings to participants’ risk status will make a difference, but there still will be considerable room for improvement in drug court outcomes,” Dr. Marlowe notes. For high-risk participants who continue to have drug or alcohol problems, the program needs further tailoring, he explains. Those who are not compliant with the program—for example, those who fail to attend counseling sessions or to deliver urine specimens—might respond to more frequent judicial supervision or to sanctions such as home curfews. In contrast, increasing the scope of treatment services might be more effective with high-risk participants who are compliant with program rules but fail to achieve abstinence because of the severity of their drug addiction or a related difficulty, such as a co-occurring mental disorder, family problems, unemployment, or homelessness. Dr. Marlowe notes that even low-risk drug offenders need more effective interventions.

DRUG COURT FREQUENCY CAN AFFECT TREATMENT OUTCOME

Participants who were considered high-risk provided more drug-free urine samples when they were required to appear in drug court every 2 weeks (square) rather than according to the standard schedule of every 4 to 6 weeks (circle). In contrast, participants who were at lower risk of relapse did comparably well on the standard schedule (open square) and when court appearances were scheduled only in response to treatment-rule infractions (triangle).



SOURCE: Marlowe, D.B., et al. Matching judicial supervision to clients’ risk status in drug court. *Crime & Delinquency* 52, 52–76, 2006.

“Dr. Marlowe is helping us fill our knowledge gap about drug courts by identifying the elements that make them effective,” says Dr. Redonna K. Chandler, chief of NIDA’s Services Research Branch. “We may eventually be able to match criminal justice supervision and treatment services to the needs of individual offenders, making

drug courts both more effective and more costeffective.” Dr. Marlowe says, “We hope that drug court programs eventually become flexible enough to allow participants doing poorly to be switched to a more intensive track and allow those doing well in an intensive program to move to a lower supervision regimen.”

Source

- Marlowe, D.B., et al. Adapting judicial supervision to the risk level of drug offenders: Discharge and 6-month outcomes from a prospective matching study. *Drug and Alcohol Dependence* 88(Suppl. 2):S4-13, 2007. **NN**

Drug Courts Add Value

Studies have shown that drug courts significantly increase the time drug abusers stay in treatment. An average of 60 percent of drug court clients complete at least 12 months of treatment, whereas only 10 percent of probationers and parolees typically remain for a year in community-based drug treatment programs, says Dr. Douglas Marlowe of the University of Pennsylvania, summarizing several research reports. A 1998 review of 13 drug court studies found that drug court clients abuse substances less frequently than comparable probationers (10 percent of urine tests were positive, compared with 31 percent). What’s more, drug courts reduce re-arrest rates by 8 to 24 percent, according to five meta-analyses in 2005 and 2006. Although drug courts tend to be more expensive than other programs, the reduction in recidivism decreases later judicial costs and financial loss to crime victims, according to a U.S. Government Accountability Office report published in 2005.* It cited net predicted benefits of \$1,000 to \$15,000 per participant.

*Adult Drug Court: Evidence Indicates Recidivism Reduction and Mixed Results for Other Outcomes, GAO-05-219, February 2005.

Reducing Postpartum Drug Use



In a recent clinical trial, a 20-minute computerized intervention reduced new mothers' drug abuse in the first 4 months postpartum. The computer software program, which was developed by Dr. Steven J. Ondersma and colleagues at Wayne State University in Detroit and Virginia Commonwealth University in Richmond, was administered in an urban obstetric hospital soon after each woman gave birth. The program features an animated narrator who asks questions, addresses ambivalence, provides feedback, and offers options. The intervention also included vouchers for an initial session of drug treatment and an easy-to-read brochure, mailed to the women after they took their babies home, that discussed infant and maternal health and briefly addressed drug abuse. The researchers estimated that the intervention had a "small to moderate" beneficial effect in their study population—107 mostly poor women who abused drugs. At a 4-month followup, those who received the intervention reported using cocaine, amphetamine, and opiates less

frequently than before the birth, while the comparison group reported slightly increased abuse of these drugs. No definitive differences were observed between the two groups regarding marijuana use.

Source

- *American Journal of Preventive Medicine* 32(3):231-238, 2007. **NN**

Lofexidine May Enhance Naltrexone Efficacy

The anti-hypertensive medication lofexidine is used commonly in the United Kingdom and less often in the United States to alleviate symptoms of opiate withdrawal. Now, a pilot study by Dr. Rajita Sinha and colleagues at Yale University School of Medicine suggests that lofexidine can enhance success rates among patients taking maintenance naltrexone to avoid relapse to opioids. The researchers stabilized 18 opioid-detoxified men and women on naltrexone (50 mg) and lofexidine (2.4 mg) daily for 1 month. They then retained all the patients on naltrexone for 4 more weeks, but kept 8 on lofexidine and gave 10 others identical-looking pills containing lofexidine doses that—unbeknownst to the patients—tapered to zero over several days. Of the 13 patients who completed the study, 80 percent of those who continued to receive combination therapy submitted opiate-free urine samples throughout the 4-week period, compared with 25 percent of those tapered to placebo. A followup laboratory session that exposed 10 of the patients to stressful and opiate-related stimuli showed that lofexidine—but not placebo—reduced the patients' reaction to stress, stress-induced opiate craving, and negative emotions (such as anger), all of which can trigger relapse.

Source

- *Psychopharmacology* 190(4):569-574, 2007. **NN**

New Therapy Reduces Drug Abuse Among Patients With Severe Mental Illness

A specially designed group intervention also improves patients' functioning in the community.

By *NIDA NOTES* Staff

A new intervention enhances prospects for substance abusers whose mental illness complicates the path to recovery. In a recent clinical trial, a 6-month course of Behavioral Treatment for Substance Abuse in Severe and Persistent Mental Illness (BTSAS) reduced drug abuse, boosted treatment-session attendance, and improved the quality of life of outpatients with a wide spectrum of mental disorders.

A Focus On Extra Obstacles

Dr. Alan S. Bellack and colleagues at the University of Maryland School of Medicine in Baltimore designed BTSAS to counter the factors that make recovery from addiction especially difficult for people who have co-occurring severe and persistent mental illness. These factors include frequent failure to meet their own and others' expectations, inconsistent motivation, and social and personal pressure to appear normal.

BTSAS therapy comprises six integrated components:

- motivational interviews (directive counseling that explores and resolves ambivalence) to increase the desire to stop using drugs;
- contingency contracts linking drug-free urine samples with small financial rewards;
- realistic, short-term, structured goal-setting sessions;
- training in social and drug-refusal skills;
- information on why and how people become addicted to drugs and the dangers of substance use for people with mental illness; and
- relapse-prevention training that inculcates behavioral strategies for coping with cravings, lapses, and high-risk situations.

Twice-weekly sessions begin with urine tests. Patients who have provided drug-free urine samples are praised by the therapists and group members. They also receive financial incentives that start at \$1.50 for the first drug-free sample and increase in \$0.50 increments for every consecutive one thereafter, up to \$3.50. The amount is set back to \$1.50 after a drug-positive sample or an absence.

When participants submit drug-positive samples, the group

TREATMENT OUTCOMES		
	BTSAS	STAR
Drug-free Urine Samples	59%	25%
Four Weeks of Abstinence	54%	16%
Multiple 4-Week Blocks	44%	10%
Eights Weeks of Abstinence	33%	8%
BTSAS: Behavioral Treatment for Substance Abuse in Severe and Persistent Mental Illness; STAR: Supportive Treatment for Addiction Recovery.		

takes a non-accusatory approach by focusing on problem solving to help them achieve future abstinence. Each participant agrees upon a personal goal for

drug abuse reduction or abstinence that he or she believes is achievable during the coming week and signs a contract stating that he or she will strive for it. The rest of the session consists of drug abuse education plus training in social skills and relapse-prevention strategies.

Superior Results

Substance abuse is common among the mentally ill. For example, surveys estimate that 48 percent of those with schizophrenia, 56 percent with bipolar disorder, and as many as 65 percent with severe and persistent mental illness have abused substances.

Dr. Bellack's research team recruited 175 patients from community clinics and a Veterans Affairs medical center in Baltimore. All had a dual diagnosis of severe and persistent mental illness and an addiction to cocaine, heroin, or marijuana. Among the participants, 38.3 percent met the diagnostic criteria for schizophrenia or schizoaffective disorders, 54.9 percent for major affective disorders, and the remainder for other mental disorders. Cocaine was the predominant drug abused by 68.6 percent of participants, opiates by 24.6 percent, and marijuana by 6.8 percent.

The researchers assigned half the trial participants to BTSAS group therapy and half to a program called Supportive Treatment for Addiction Recovery (STAR), which is the typical treatment at the University of Maryland clinics. Unlike participants in BTSAS, those in STAR do not follow a structured format but instead select their own topics and work at their own pace. Patient

interaction with other patients is encouraged but not required as it is with BTSAS. Although urine samples are collected before each session, results are not discussed in the group, and no systematic feedback is provided to the patient.

Assignments to the BTSAS and STAR groups were balanced for gender, psychiatric diagnosis, type of drug dependency, and number of substance use disorders. Treatment groups of four to six participants met twice a week for 6 months. BTSAS and STAR group sessions were all led by trained therapists and lasted from 60 to 90 minutes. Group meetings were videotaped weekly and then reviewed and assessed by independent reviewers to verify that the therapists were following the programs' parameters correctly.

The BTSAS group fared better than the STAR group on a wide range of treatment-related criteria. For example, more people in the BTSAS group stayed in treatment throughout the 6-month trial period (57.4 percent versus 34.7 percent). The BTSAS group produced more drug-free urine samples and had longer periods of abstinence (see table). They also had better clinical and general living outcomes than people in the STAR group (see table, below) and reported larger improvements in their ability to perform the activities of daily living.

"It was apparent from watching videotapes of treatment sessions that subjects in BTSAS valued the intervention and were learning important skills for reducing drug use," says Dr. Bellack. "We were very gratified that the data supported our clinical observations."

The researchers reported that the extra costs of running the BTSAS program were modest. For the 6-month trial, monetary rewards averaged roughly \$60 per patient; total per-patient cost, including therapist time, was \$372.

Ongoing Refinements

The trial data indicate that patients who remain in BTSAS for at least three sessions are much more likely to finish

QUALITY-OF-LIFE OUTCOMES				
	BTSAS		STAR	
	Pretreatment*	Posttreatment**	Pretreatment	Posttreatment
Frequency of Arrests	31.0%	12.8%	22.9%	27.3%
Inpatient Admissions***	29.5%	6.5%	20.4%	16.2%
Living Standards****	46.6%	69.2%	43.8%	51.5%
*Pretreatment: 90-day period before study **Posttreatment: 90-day period following study ***Rates of inpatient admissions for either psychiatric problems or substance abuse ****Percentage of participants reporting having enough money for food, clothing, housing, and transportation				

the 6-month program than patients who do not make it through the third session. Because a third of individuals initially recruited for the study left before the third treatment session, the researchers are currently developing new intervention strategies to keep people in the program until they have truly given it a chance. The innovation has two key components: a structured intervention to help patients overcome obstacles to treatment and an intervention to enlist family and friends as partners to connect patients with treatment.

"The BTSAS program will help clinicians make a difference in the lives of a very difficult-to-treat population," says Dr. Dorynne Czechowicz of NIDA's Division of Clinical Neuroscience and Behavioral Research. "One of its key strengths is that it positively affects many aspects of patients' lives. Moreover, as an outpatient treatment, it is well-suited to the situation. Most mentally ill people who abuse drugs live in the community, not in a sheltered facility, and this is where the majority of clinicians must treat them."

Sources

- Bellack, A.S., et al. A randomized clinical trial of a new behavioral treatment for drug abuse in people with severe and persistent mental illness. *Archives of General Psychiatry* 63(4):426-432, 2006.
- Kinnaman, J.E., et al. Assessment of motivation to change substance use in dually-diagnosed schizophrenia patients. *Addictive Behaviors* 32(9):1798-1813, 2007. **NN**

Combination Treatment Extends Marijuana Abstinence

Vouchers provide a strong incentive for abstinence during treatment, and cognitive-behavioral therapy helps patients maintain abstinence after treatment ends.

By Debra P. Davis, *NIDA NOTES* Senior Editor

Treatment that combines vouchers and cognitive-behavioral therapy (CBT) may be more effective in keeping marijuana abusers abstinent in the longer term than vouchers-only and CBT-only programs. In a study by Dr. Alan Budney and colleagues at the University of Vermont, vouchers alone generated the longest periods of abstinence during 14 weeks of treatment, while vouchers and CBT in combination yielded superior abstinence during a 12-month posttreatment period.

"This is our second study demonstrating that an abstinence-based voucher program can increase positive outcomes for folks seeking treatment for marijuana dependence," says Dr. Budney, who is now at the University of Arkansas for Medical Sciences. "It provides evidence that vouchers used as adjuncts to traditional behavioral therapy can improve outcomes."

The current study extended the earlier one by including post-treatment assessments. Vouchers provided a strong incentive for abstinence during treatment, as they did in the earlier study, but the effect of vouchers alone did not hold up as well as the combined treatment once the program ended. The higher posttreatment abstinence rates for the combined treatment relative to the vouchers-only treatment suggest that the behavioral therapy helped to maintain the effect of the vouchers, Dr. Budney says. He

attributes this maintenance effect to the coping skills and motivational training provided by the CBT.

For the study, 90 adults (69 men, 21 women) seeking treatment for mari-

juana dependence at a university-based outpatient clinic in Burlington, Vermont, were randomly assigned to treatment with vouchers (30), CBT (30), or both (30). Most were smoking marijuana daily and presenting themselves for treatment for the first time; their average length of marijuana abuse was 14 years. Each time a participant in the vouchers-only or combination treatment submitted a marijuana negative urine sample, he or she received a voucher worth \$1.50; a second consecutive negative sample earned \$3.00, a third \$4.50, and so on. In addition, each consecutive pair of negative samples netted a bonus voucher worth \$10. A full 14-week run of weekly drug-free samples would net vouchers worth \$570, which were redeemable for retail goods or services.

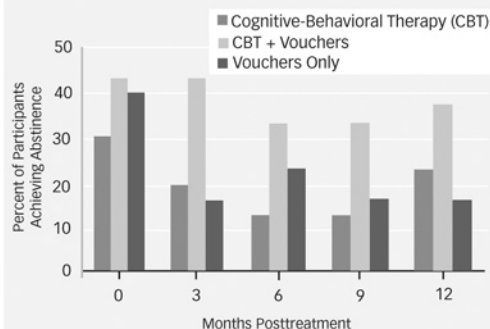
The CBT included 50-minute weekly sessions involving motivational counseling, drug refusal, and coping skills. To encourage cooperation with the urine screens and help equalize retention and treatment contact across the groups, researchers paid the CBT-only participants \$5 in vouchers each time they showed up for a screen, regardless of their test results. Complete adherence to the sessions and screens would earn \$140 over the 14-week period.

During treatment, vouchers-only patients produced the most marijuana-negative urine specimens (55 percent versus 43 percent for combined treatment and 32 percent for CBT only), weeks of continuous abstinence (mean 6.9 versus 5.3 for combined treatment and 3.5 for CBT only), and continuous abstinences lasting 6 or more weeks (50 percent versus 40 percent for combined treatment and 17 percent for CBT only). In addition to duration of abstinence, researchers measured days of self-reported marijuana abuse, changes in marijuana-related problems, and psychosocial outcomes. Participants in all three groups showed similar improvements in these areas at the end of treatment (see chart).

Combined Treatment Benefits

At the end of treatment and at each of four quarterly followups, patients who received the combined treatment had the highest abstinence prevalence, averaging 38 percent over the 12 months, compared with 23 percent for vouchers only and 20 percent for CBT only. The combined treatment group also had the highest rate of contin-

COMBINED TREATMENT HELPS MAINTAIN ABSTINENCE Over the 12 months following treatment, abstinence levels for all treatment conditions tended to decline, but levels for the combined treatment remained consistently higher than those for CBT or vouchers only.



uous abstinence throughout treatment and followup, 37 percent, compared with 30 percent for CBT and 27 percent for vouchers. On average, patients who received the combination treatment used marijuana 13 days out of 30 during followup, compared with 18 days among patients who received the single treatments.

“The findings of this study show that vouchers are effective in producing initial abstinence during treatment,” says Ms. Debra Grossman of NIDA’s Division of Clinical Neuroscience and Behavioral Research. “The addition of cognitivebehavioral therapy did not enhance initial abstinence, but helped maintain abstinence and produced better long-term outcomes. These findings are consistent with other studies.” In two previous studies with cocaine abusers, vouchers alone performed as well as vouchers plus CBT during treatment. One of the studies indicated that CBT augmented the effects of the vouchers during the posttreatment period.

Dr. Budney says his team set the value of the vouchers arbitrarily, with the aim of keeping costs down; he believes bigger payoffs would produce better outcomes. The escalating values for consecutive negative urine samples progressively strengthened the incentive for participants to avoid lapses; each time a participant submitted a positive sample or missed a screening, the reward for the next negative sample reverted to the original \$1.50 voucher. Dr. Budney suggests that future studies might cut costs by incorporating behavioral therapy only at key points in the treatment, rather than weekly throughout. In the researchers’ experience, such a point often comes in the fourth to sixth week of abstinence, when patients may start to lose motivation and become vulnerable to relapse.

Fewer than half of the participants in Dr. Budney’s study had positive outcomes, indicating that more effective treatments are needed for marijuana dependence. “Despite the promising findings, the majority of patients are not being sufficiently helped, and thus we need continued research focused on maximizing the outcome,” Ms. Grossman notes. “Marijuana is the most commonly used

VOUCHERS BOOST ABSTINENCE RATES DURING TREATMENT Participants in the vouchers-only group had better abstinence outcomes than those in the combination or CBT-only groups during treatment. All three groups reported substantial improvements over the 14-week period, but no significant intergroup differences, on measures such as the number of days participants used marijuana and how often they experienced marijuana-related problems.

	CBT	CBT+V	V
Primary abstinence outcomes			
Mean weeks of continuous abstinence ^a	3.5	5.3	6.9
% of participants who achieved 6 or more weeks of continuous abstinence ^{a,b}	17.0	40.0	50.0
% marijuana-negative urine specimens	32.0	43.0	55.0
Secondary self-report measures			
Number of days marijuana used during prior month ^c			
Intake	26.1	24.8	25.8
End of treatment	8.6	9.7	11.3
Number of times marijuana used per day ^c			
Intake	3.7	4.2	3.8
End of treatment ^a	1.6	2.7	2.6
Marijuana Problem Scale ^c			
Intake	7.9	7.8	7.8
End of treatment	5.1	3.6	4.1
<small>Data for all analyses were based on all participants (n = 30 per treatment condition). Mean data reflect means adjusted for abstinence prior to treatment. ^aCBT vs. V, comparison $p < .05$ ^bCBT+V vs. CBT, comparison $p < .05$ ^cSignificant main effect for time, $p < .01$ </small>			

illegal drug in the United States, yet among the least studied, and treatment based on abstinence-based vouchers has been found to be effective for other drugs of abuse.”

Source

- Budney, A.J., et al. Clinical trial of abstinence-based vouchers and cognitive-behavioral therapy for cannabis dependence. *Journal of Consulting and Clinical Psychology* 74(2):307-316, 2006. **NN**

Sertraline Does Not Help Methamphetamine Abusers Quit

Selective serotonin reuptake inhibitors do not relieve the depressive symptoms of methamphetamine withdrawal and may produce unpleasant side effects.

By Elizabeth Ashton, *NIDA NOTES* Staff Writer

In a recent NIDA-funded study, the antidepressant sertraline (Zoloft) made quitting methamphetamine harder. Prescribed to relieve depression during the methamphetamine withdrawal process, sertraline produced a number of unpleasant side effects and may have interfered with behavioral interventions as well.

Dr. Steven Shoptaw, Dr. Alice Huber, Dr. Walter Ling, and their colleagues at the University of California, Los Angeles (UCLA) noted that methamphetamine abusers in withdrawal frequently complained of fatigue, lack of pleasure, sad mood, and persistent daytime sleepiness. The researchers hypothesized that the sertraline might alleviate these symptoms and promote abstinence because:

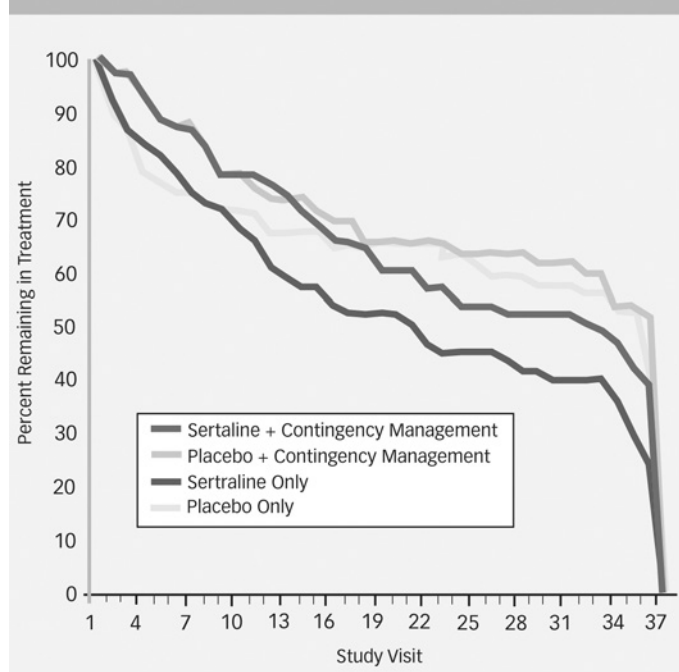
- methamphetamine is toxic to several pathways that produce the neurotransmitter serotonin;
- sertraline belongs to a class of antidepressant medications, the selective serotonin reuptake inhibitors (SSRI), that treat major depression by raising serotonin levels in the brain.

Hypothesis Disproved

The team recruited 229 men and women who were addicted to methamphetamine. All were between the ages of 18 and 65, and all were seeking treatment. The trial began with a 2-week preparation process. The researchers performed baseline testing and encouraged the participants to stop taking methamphetamine with the help of twice-weekly recovery skills groups. At the end of 2 weeks, they randomly assigned the participants to one of four groups: sertraline with contingency management (CM), sertraline alone, placebo with CM, and placebo alone. All participants provided urine samples on Mondays, Wednesdays, and Fridays and attended a 90-minute psychological support group three times a week based on the Matrix Model relapse prevention program. This standardized, manual-driven model is evidence-based and incorporates social learning, behavioral and cognitive therapies, and psychological and HIV-risk education.

The researchers evaluated methamphetamine use, time spent in the program, methamphetamine craving, and depressive symptoms. They found that:

A TREATMENT FAILS THE TEST Participants receiving sertraline alone stayed in treatment for significantly less time than participants in all other treatment conditions.



- more participants in the CM program achieved 3 consecutive weeks of abstinence than participants who were not in the CM program (47 vs. 33 percent); all participants who received CM benefitted from this therapy, but its positive effects were blunted in the sertraline-with-CM group.
- fewer participants on sertraline alone, as compared with those on placebo alone (34 percent vs. 47 percent), achieved the goal of at least 3 consecutive drug-free urine samples during the study's 12-week treatment phase; participants on sertraline alone also attended fewer relapse prevention sessions and were more likely to drop out.
- craving and depressive symptoms were affected only by time since the last methamphetamine dose, and neither sertraline nor CM changed either of these two measures.

In addition, the sertraline group reported significantly more sexual, gastrointestinal (including nausea), and anticholinergic side effects.

Rethinking Withdrawal Support

The researchers concluded that treatment with sertraline did not relieve the depression associated with methamphetamine withdrawal or decrease methamphetamine use, and its side effects reduced the amount of time participants spent in treatment. Those who took sertraline also seemed to benefit less from behavioral interventions, and the researchers speculated that this might be due to the dampening effect of the medication since they had excluded all other possible factors in the statistical analysis.

The team recommends that clinicians not give SSRIs to people withdrawing from methamphetamine unless an underlying primary depressive disorder is definitively diagnosed. The recommendation reflects their own results and those of previous smaller studies with fluoxetine (Prozac) and paroxetine (Paxil), both of which were also found to have no effect on depressive symptoms during methamphetamine withdrawal. Together, these findings suggest that the etiology of mood disorder during methamphetamine withdrawal differs from that of primary depression.

The UCLA researchers suggest that clinicians offer people addicted to methamphetamine an effective behavioral intervention for depressive symptoms during the withdrawal process before prescribing any of the currently available pharmacotherapies for depression. If medication is needed, only non-SSRI antidepressants, such as bupropion, should be used.

“The SSRI sertraline is not only inefficacious for the treatment of methamphetamine dependence, but also produces a number of unprecedented side effects and has no effect on the secondary depression experienced during methamphetamine withdrawal,” says Dr. Ivan Montoya, Clinical Director of NIDA’s Pharmacotherapies and Medical Consequences of Drug Abuse Branch. “In addition, the negative effects of this SSRI in methamphetamine users are so powerful that they can dampen the strong therapeutic effects of contingency management. If these reactions can be traced to their source, they may help us understand the extent and duration of the effects of methamphetamine on the brain.”

“We are trying to determine what people withdrawing from methamphetamine need to make withdrawal easier,” Dr. Shoptaw says. “We’ve figured this out for other drugs, such as cocaine and heroin, but finding medications that counter the withdrawal symptoms of methamphetamine addiction is still a work in progress. We need this information so we can design treatment programs that help people get off and stay off this damaging drug.”

Source

- Shoptaw, S., et al. Randomized, placebo-controlled trial of sertraline and contingency management for the treatment of methamphetamine dependence. *Drug and Alcohol Dependence* 85(1):12-18, 2006. **NN**

Chronic Cocaine Abusers Have Occult Insomnia in Early Abstinence

Patients in early treatment may not recognize their own sleep impairment or its impact on their performance.

By Lori Whitten, *NIDA NOTES* Staff Writer

Chronic cocaine abusers may feel they are sleeping better and better during early abstinence, but objective measures show the opposite happens. A team of NIDA-funded addiction and sleep researchers at the Yale and Harvard Schools of Medicine found evidence of insomnia, with learning and attentional deficits, on days of taking the drug and after 2.5 weeks of abstinence. The researchers believe cocaine may impair the brain's ability to gauge its own need for sleep, and patients' ability to benefit from early treatment may suffer as a result.

"Problems in memory and attention are linked with increased treatment dropout and likely affect patients' ability to 'take in' lessons from drug abuse counseling," says Dr. Robert Malison of Yale, a co-investigator on the study. If the results are confirmed, clinicians and patients may want to consider addressing sleep disorders in early therapy, perhaps with the use of medications or behavioral treatments.

The researchers recruited 10 men and two women aged 24 to 49 who, on average, had abused cocaine for 17 years and had used \$500 worth of the drug per week. All the participants declined an offer of drug abuse treatment. Urine tests indicated that cocaine was the only drug any of them had abused during the week before the study.

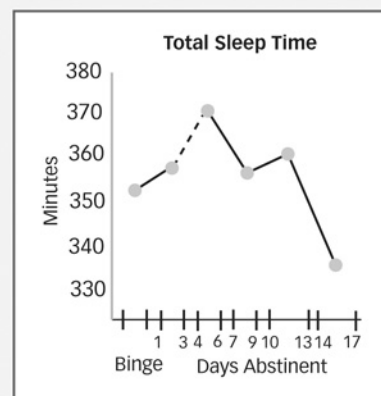
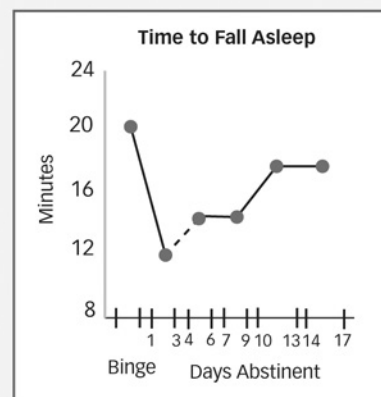
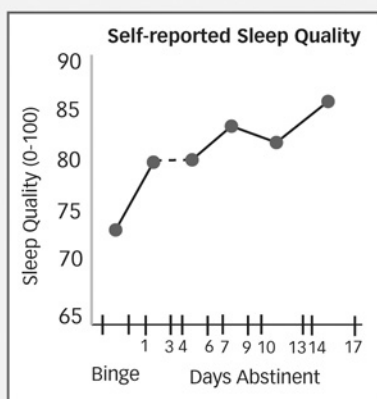
At the outset of the study, participants self-administered cocaine from a pump under physician oversight, building up to a dose of 32 mg/kg of body weight over 1.5 hours, then repeating this dose essentially at will, but no less than 5 minutes apart, for another 1.5 hours. Subsequently, they self-administered the higher dose with the same minimal restriction for 2 hours on each of three consecutive days, either on days 4-6 or 18-20. This schedule simulated chronic cocaine abusers' typical bingeing pattern of drug abuse and allowed researchers

to monitor each participant's sleep and cognitive performance for 17 days after a binge.

Research staff made sure the participants stayed awake from 7:45 AM to 9:30 PM, and let them sleep through the night. At night, the participants wore Nightcap sleep monitors, a bandana-like device that records eye and body movements that indicate whether someone is awake, asleep and dreaming, or sleeping dreamlessly. On most nights participants also wore polysomnographic (PSG) devices that continuously assessed brain activity with electroencephalography (EEG) and measured eye and

OBJECTIVE MEASURES BELIE PATIENTS' IMPRESSIONS OF SLEEP IMPROVEMENT

Patients thought their sleep was better (left), but objective measures (right) showed that after an initial improvement they started to need longer to fall asleep and their total sleep time went down.

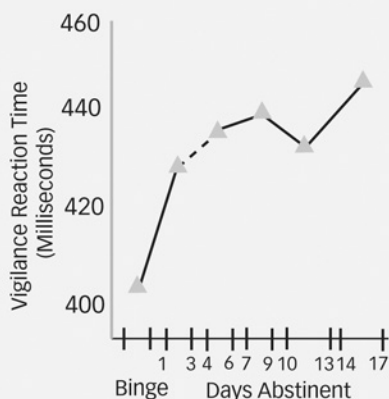


muscle movements associated with different sleep stages. Combining the information gathered by these measures with participants' responses to daily questionnaires on their sleep experience and with cognitive testing, the researchers demonstrated that the participants had:

- *Sleep deficits*—After 14 to 17 days of abstinence, the study group exhibited sleep deficits on several measures, relative to healthy, age-matched peers who participated in prior studies. For example, they had less total sleep time (336 versus 421-464 minutes) and took longer to fall asleep (19 versus 6-16 minutes).
- *Declines in sleep quantity and quality*—The time participants took to fall asleep and their total time asleep transiently improved during the first week of abstinence, but then reverted to the patterns recorded on days of cocaine taking. On abstinence days 14-17, participants took an average of 20 minutes to fall asleep (from a low of 11) and slept for 40 minutes less than their minimum. Slow-wave sleep—a deep sleep that often increases following sleep deprivation—rose during the binge and on abstinence days 10-17.
- *Lack of awareness of their sleep problems*—In contrast to the evidence of objective measures, the study participants reported steadily improving sleep from the beginning to the end of their days of abstinence.
- *Impairments in learning and attention*—As with sleep quality, participants' performance on tests of alertness and motor-skills learning initially improved and then deteriorated. On abstinence day 17, they registered their lowest scores on alertness and ability to learn a new motor skill.

ALERTNESS IMPAIRMENTS PARALLEL SLEEP DEFICITS

In the Digital Vigilance Test, participants were required to press a button when they saw a target number on the right side of the screen while viewing a rapidly changing number sequence in the middle of the screen. Poor performance on the task corresponded with sleep deficits at 14-17 days of abstinence.

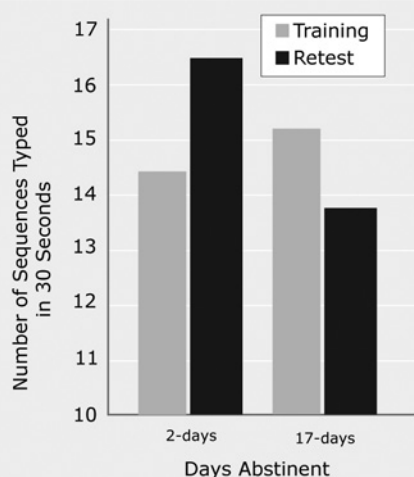


Increased Risk of Relapse

“Unlike most people with chronic insomnia, including alcoholics, cocaine abusers do not perceive sleep problems and may not ask clinicians for treatment to improve sleep,” says Dr. Malison. The problem often goes unaddressed and persists as a result, and the accompanying impair-

PERFORMANCE DECLINES WITH SLEEP QUALITY

In the Motor-Sequence Task, participants typed a five-digit sequence of four keys with their non-dominant hand, a skill that improves after a night's sleep. Cocaine abusers showed improvement after two but not 17 days of abstinence.



ments in attention and learning may affect how well they respond to drug abuse treatment (see “Cocaine Abusers’ Cognitive Deficits Compromise Treatment Outcomes”). Clinical studies have shown that poor objective sleep during the first 2 weeks of abstinence predicts relapse to alcohol 5 months after treatment.

In fact, the insidious nature of cocaine-related insomnia may

directly trigger relapse, suggests Dr. Peter Morgan, lead investigator of the study. “Addicted people may take cocaine to improve sleep-related cognitive functioning deficits—unaware that they are abusing, in part, to ‘solve’ these problems.”

Dr. Morgan adds, “Cocaine abusers who recognize their cognitive problems often report that it takes them 6 months to a year to turn the corner—a clinical observation that points to the need for longer term studies of sleep and treatment outcomes among this population.” In addition to studies with larger numbers of participants, the investigators say there is a need to investigate possible gender differences in cocaine-related sleep problems. Dr. Morgan and his team are currently testing two medications, tiagabine and modafinil, to see if they can improve cocaine abusers’ sleep and restore cognitive performance.

“Experts believe that not getting enough sleep is an unmet public health problem in the general population. These findings highlight this important problem in cocaine abusers,” says Dr. Harold Gordon of NIDA’s Division of Clinical Neuroscience and Behavioral Research.

Source

- Morgan, P.T., et al. Sleep, sleep-dependent procedural learning and vigilance in chronic cocaine users: Evidence for occult insomnia. *Drug and Alcohol Dependence* 82(3):238-249, 2006. **NN**

Bupropion Reduces Meth's Subjective Effects and Cue-Induced Craving

A small placebo-controlled trial produced evidence that the antidepressant bupropion may be useful for treating methamphetamine addiction. Drs. Thomas Newton and Richard De La Garza at the University of California, Los Angeles, and Dr. John Roach and colleagues, at the University of Texas, San Antonio, divided 20 methamphetamine-addicted individuals into two groups for 6 days of treatment: one group received bupropion (150 mg/d) throughout the trial and the other, placebo. At baseline and the end of the trial each participant received three infusions; one of an inert vehicle and two of methamphetamine (15mg and 30 mg), spaced over 2 hours. Before and at frequent intervals after each infusion, participants reported on their subjective reactions. Compared to baseline, those who received bupropion experienced reduced highs and slightly decreased cravings at the end of the trial, while those who received placebo experienced significantly more craving.

Source

- *Neuropsychopharmacology* 31(7):1537-1544, 2006. **NN**

NIDA's Newest Division Mines Clinical Applications From Basic Research

NIDA's Division of Clinical Neuroscience and Behavioral Research

By Debra P. Davis, *NIDA NOTES* Staff Writer

NIDA's Division of Clinical Neuroscience and Behavioral Research (DCNBR) identifies, validates, and explores the clinical implications of basic science discoveries. Much of the Division's work consists of replicating results obtained in laboratory and animal studies in human subjects. A DCNBR project typically culminates in one of two outcomes: carrying a new discovery forward for development into actual interventions or referring it back to basic scientists for further investigation.

"We are uniquely positioned to uncover the factors in humans—neurobiologic, genetic, social-behavioral—that help explain the development and effects of drug abuse," says Director Dr. Joseph Frascella. "Being positioned between NIDA's basic research division and other more applied programs, our research programs inform basic science and promote the development and implementation of new medications and behavioral treatments across NIDA."

For example, building on basic research that linked nicotine acetylcholine receptors to the regulation of attention, DCNBR-sponsored researcher David Gilbert and colleagues at Southern Illinois University demonstrated that nicotine exposure and smoking cessation both influence the ability to pay attention. Now, NIDA's Division of Pharmacotherapies and Medical Consequences of Drug Abuse is exploring the clinical impact of these observations. They are testing whether bupropion and nicotine patches affect attention during smoking cessation, and whether such effects correlate with success in quitting.

In another DCNBR-supported study, Dr. Robert Risinger and colleagues at the Medical College of Wisconsin documented a pattern of fluctuating activation of the mesolimbic reward system as six cocaine-abusing men transitioned through cycles of cocaine craving, self-administration, and highs. The results, obtained with functional magnetic resonance imaging (fMRI), confirmed previous research linking those brain areas to drug self-administration in animals, and extended them by correlating them with drug abusers' subjective feelings and responses. (see "Cocaine Craving Activates Brain Reward Structures; Cocaine 'High' Dampens Them," *NIDA NOTES*, Vol. 21, No. 2).

Neuroimaging studies comprise onethird of the Division's research portfolio. "Brain imaging has pushed drug abuse research in the last 15 to 20 years—allowing us to directly observe neural activity of awake and functioning people and obtain specific measures on how drugs affect the brain," Dr. Frascella says. Imaging studies indicate that the human brain undergoes major changes as a consequence of drug exposure and that the adolescent brain may be particularly pliant, "which may help explain why adolescence is the period when most new cases of drug addiction occur," Dr. Frascella adds. "Thus, we've become increasingly committed to using brain imaging to get a sharper picture of how the brain changes with development and in response to active and passive exposure to drugs of abuse."

Three Branches of Clinical Research

DCNBR, formed in May 2004, has three Branches:

Clinical Neuroscience: Under Dr. Steven Grant's leadership, the Clinical Neuroscience Branch focuses on how drug abuse affects the human central nervous system, including brain changes during different stages and states of abuse, such as addiction, withdrawal, abstinence, craving, and relapse. It also studies:

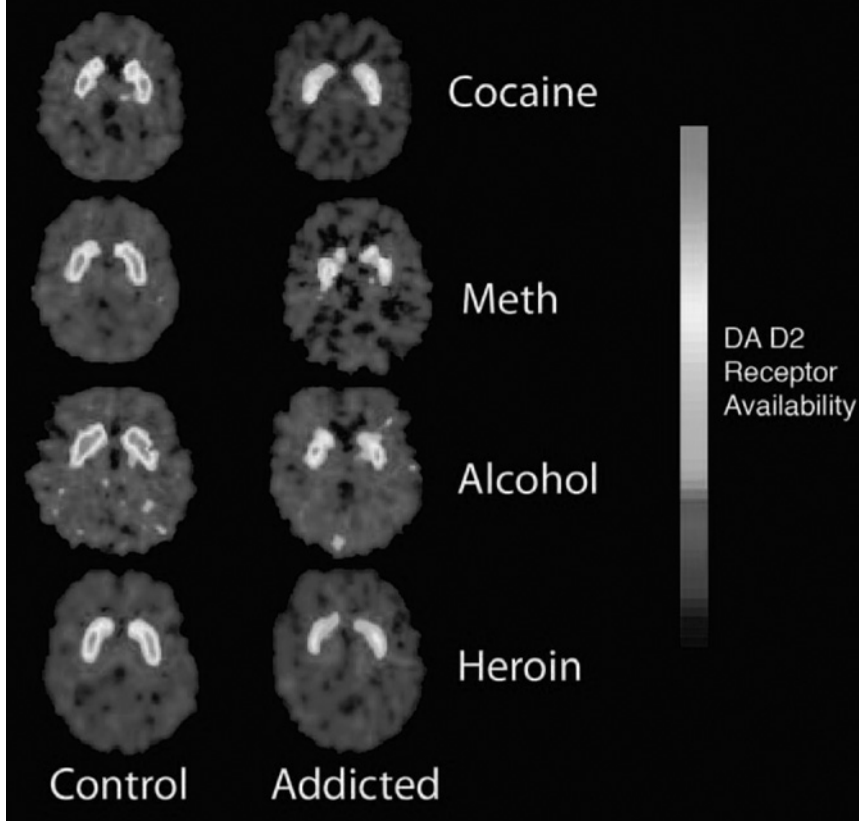
- The factors that make some individuals more vulnerable and others more resilient to drug abuse and addiction;
- The impact of drugs on learning, memory, judgment, and decision-making;
- Co-occurrence of drug addiction with other mental disorders;
- Neurobiological changes that result from behavioral and pharmacological treatments for drug abuse; and
- Interventions to ameliorate the negative health consequences of drugs, whether self-administered or incurred prenatally.

As an example of a recent Branch achievement, Dr. Grant points to a study by Dr. Martin Paulus and colleagues at the University of California, San Diego.

BRAIN IMAGING IS A KEY TOOL IN STUDIES SPONSORED BY THE DIVISION OF CLINICAL NEUROSCIENCE AND BEHAVIORAL RESEARCH

The images below—used in a recent Division presentation—show that repeated exposure to drugs depletes the brain's dopamine receptors, which are critical for one's ability to experience pleasure and reward.

Dopamine D2 Receptors Are Lower in Addiction



The researchers performed fMRI while 46 men who had been abstinent from methamphetamine for about a month took a decisionmaking test. The researchers found that patterns of activation in certain brain regions predicted with high accuracy which men would and would not relapse 1 year later (see “Brain Activity Patterns Signal Risk of Relapse to Methamphetamine,” *NIDA NOTES*, Vol. 20, No. 5). “This use of fMRI, if replicated, could be adapted for treatment and preventive interventions,” Dr. Frascella says.

Behavioral and Brain Development: Led by Dr. Vincent Smeriglio, this Branch examines drug exposure and abuse, and their health and social consequences, through the course of human development—from the prenatal period through childhood, adolescence, and young adulthood. Research focuses on:

- The effects of drugs on behavioral and brain development;

- The role of genetic, neurobiological, and environmental factors in youths’ vulnerability to drug abuse and addiction; and
- The developmental effects of cooccurring exposure to drugs and infectious diseases as well as the impact of drug abuse on youths with mental illness.

One theme of the Branch’s work is research to tailor drug abuse treatments to individual needs. As a recent example, a Branch-supported study by Dr. Leslie Jacobsen and colleagues at Yale University School of Medicine found that adolescent smokers experienced greater memory impairment during nicotine withdrawal if their mothers had smoked while pregnant. The study also produced fMRI evidence implicating particular brain regions in the deficits, which may be useful diagnostically as well as therapeutically.

Behavioral and Integrative Treatment:

This Branch, under Dr. Lisa Onken’s direction, aims to develop new and improved treatments for drug abuse and addiction, including behavioral, combined behavioral-pharmacological, and complementary and alternative treatments. The Branch designs new interventions, tests them for efficacy, and evaluates strategies to improve treatment engagement, adherence, and retention—key factors in success. The Branch also supports research that prepares treatments for use in community settings, where cost, training, and fit with existing services can be constraints.

“Behavioral therapies that work well in a research setting cannot necessarily be taken into the community. Oftentimes, they are too complicated and expensive, and require extensive training for clinicians,” Dr. Frascella notes. One way of developing a community-friendly treatment is to identify the active ingredients of effective treatments, explains Dr. Onken. “In this way, we may be able to create more streamlined treatments that retain their potency. Another novel approach to making a treatment more community-friendly is to use computers to help counselors deliver treatment. For example, Dr. Kathleen Carroll at Yale University is testing the efficacy of computer-assisted cognitive-behavioral therapy in preventing cocaine relapse. **NN**

Standard Treatments Help Depressed Smokers Quit

As smoking rates fall in the United States, mentally ill individuals comprise a larger percentage of people who continue to light up.

By Lori Whitten, *NIDA NOTES* Staff Writer

Smoking cessation interventions that are effective in the general population also help for depressed smokers, suggests a study of outpatients at four mental health clinics. Dr. Sharon Hall and colleagues at the University of California, San Francisco; the University of Rhode Island; and Kaiser Permanente Northern California found that depressed smokers who were treated with a combination of motivational counseling, nicotine patches, and behavioral therapy were more likely than their counterparts who did not receive the interventions to be smoke-free at 12- and 18-month assessments.

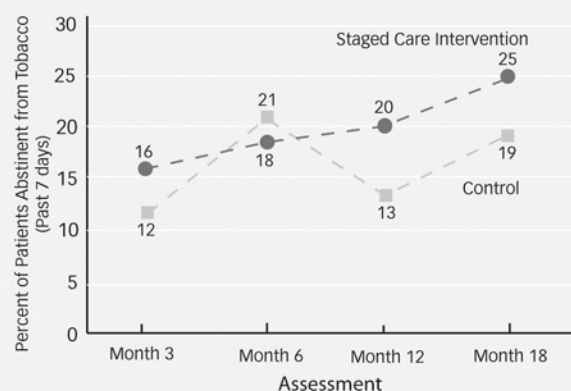
"Patients in our study mirrored the general population of smokers in their readiness to quit, acceptance of treatment, and cessation outcomes—findings that surprised me and my colleagues," says Dr. Hall, lead investigator of the study. Further, patients with severe symptoms of depression both accepted the interventions and benefited from them. "Our findings suggest that clinicians should offer depressed outpatients nicotine addiction treatment and should start with available smoking cessation interventions. They need not be overly concerned about patients' levels of depression," says Dr. Hall.

The investigators recruited 322 men and women from a university-based clinic and three sites of a health maintenance organization who were being treated for depression and smoked daily. Most of the volunteers (79 percent) were taking psychiatric medication for moderate depression. On average, they had smoked for 24 years, smoked 15 cigarettes a day, and had tried to quit six times.

At the start of the study, the participants provided information on their depression severity and treatment, smoking behavior (confirmed by expired air carbon monoxide measurements), nicotine dependence level, readiness to quit smoking, previous quit attempts, and commitment to abstinence. They repeated these self-reports 3, 6, 12, and 18 months later.

The active intervention in the study was Staged Care Intervention (SCI). At the outset and months 3, 6, and 12, participants assigned to SCI answered a computerized questionnaire about smoking, its advantages and disadvantages, triggers for smoking-related thoughts and behaviors, and ways to change these thoughts and behaviors. The computer provided an individualized feedback

MORE DEPRESSED SMOKERS QUIT WITH STAGED CARE INTERVENTION Among smokers in outpatient treatment for depression, more who participated in the Staged Care Intervention achieved abstinence at the 12- and 18-month followups compared with participants in the control group.



report that the patients and counselors reviewed together in a 15-minute session. The report classified each patient's readiness to quit based on the Stages of Change model, compared his or her responses with those of others in the program, showed changes from earlier reports, and identified triggers for smoking and strategies to move to the next stage. If the patient expressed a desire to quit, he or she began an 8-week cessation treatment. Each participant in the control group received a self-help guide to smoking cessation and a list of programs in the area, but no therapeutic contact or advice about smoking cessation.

Opportunity to Engage

About one-third (34 percent) of SCI participants entered cessation treatment. They received nicotine patches (7, 14, or 21 mg, depending on level of smoking and week of study) and six 30-minute counseling sessions. The focus of counseling was immediate and complete cessation at an agreed-upon date. During sessions, patients developed a commitment to abstinence, established a quit plan, identified reasons for smoking, reviewed the benefits of quitting, and received information on nutrition and exercise. Patients who did not attain abstinence with nicotine patches were prescribed bupropion if their mental health care provider deemed it medically appropriate.

The researchers included all SCI participants, including those who did not enter cessation treatment, in their data analysis. At the 12-month assessment, 20 percent of participants in the SCI group and 13 percent in the control group had verified 7-day tobacco abstinence. The SCI group's advantage persisted at the 18-month assessment (25 percent versus 19 percent). More SCI (44 percent) than control group participants (34 percent) endorsed permanent abstinence—an attitude the researchers say predicts success in changing behavior. The intervention was particularly effective for heavy smokers: Among participants who smoked more than a pack of cigarettes a day, those assigned to SCI were about twice as likely as controls to report a quit attempt during the study.

“The findings of Dr. Hall and her colleagues suggest that, even among severely depressed smokers who are not motivated to quit, the SCI increases abstinence rates compared with a standard control,” says Ms. Debra Grossman of NIDA's Division of Clinical Neuroscience and Behavioral Research. The finding adds to the justification for American Psychiatric Association and Agency for Health Care Research and Quality recommendations to offer smoking cessation therapy to people with mental disorders.

“The high prevalence of smoking in mental health clinics presents an opportunity to engage people with depression in smoking cessation,” says Dr. Hall. She adds that one advantage to doing so is the supportive environment of such settings: if cessation worsens depression, then patients can obtain additional help. Dr. Hall notes that

Computer Feedback Nurtures Change

Excerpts from two feedback reports illustrate individualized care:

Feedback for a person who has no immediate intention to stop smoking: Your answers on the last survey show that you need to begin to change the way you look at yourself as a smoker. You can do this by thinking more about your attitudes and beliefs about your smoking. For example:

- If you think smoking could be bad for your health, be specific about how smoking is affecting you. (For example: Cigarettes give me a sore throat—or cause my cough—or make me feel tired all the time.)
- How would your life change if you quit? (For example: I would set a better example for others—or I'd have more money to spend on things I enjoy.)
- What might be difficult if you quit? Can you plan in advance how you will handle those difficulties? (For example: I could get more exercise so I won't gain weight.)

Feedback for a person who intends to quit in the next 6 months: You seem to be well aware of the risks of smoking ... you're doing as well as others who have used this program to help themselves quit smoking! To make more progress:

- Weigh the “pros” and “cons” of smoking;
- Learn more about quitting; and
- Keep thinking of how you're doing.

the treatment benefits seen among the study population of mostly employed patients enrolled in a health maintenance organization might not apply to depressed people who are disadvantaged or in treatment at publicly funded hospitals. Dr. Hall's team plans to conduct a cost-effectiveness analysis of the intervention to help clinic directors decide on resource allocation.

Source

- Hall, S.M., et al. Treatment for cigarette smoking among depressed mental health outpatients: a randomized clinical trial. *American Journal of Public Health* 96(10):1808-1814, 2006. **NN**

Depot Naltrexone Appears Safe and Effective for Heroin Addiction

A long-lasting, injectable formula of naltrexone performed well in a pilot clinical trial.

By Sarah Teagle, *NIDA NOTES* Contributing Writer

In a NIDA-supported pilot study, a new formulation of naltrexone that patients receive by injection once every 30 days appeared safe and helped heroin-addicted outpatients persevere in treatment. Investigators observed a dose-dependent relationship between the medication, called depot naltrexone, and patient retention rates.

Naltrexone helps patients overcome urges to abuse opiates by blocking the drugs' euphoric effects. Some patients do well with it, but the oral formulation, the only one available to date, has a drawback: It must be taken daily, and a patient whose craving becomes overwhelming can obtain opiate euphoria simply by skipping a dose before resuming abuse.

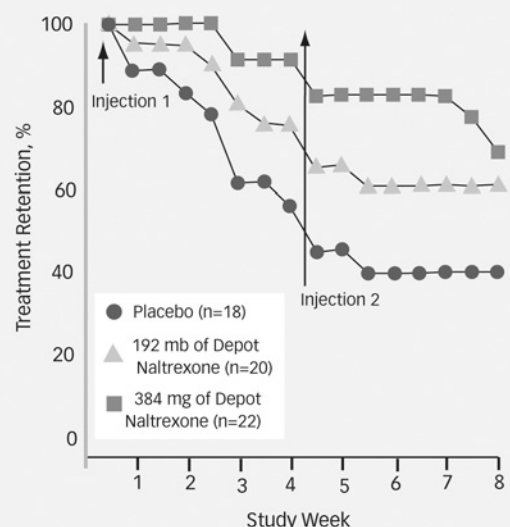
"What's exciting about this slow-release formula is that it provides continuous protection for a month at a time, freeing patients from having to decide to take or not take the medication every day," says Dr. Sandra Comer, lead investigator of the study. "By increasing treatment retention, depot naltrexone may allow patients greater contact with appropriate supportive counseling and ease their transition to a life without heroin."

Dr. Comer and her collaborators recruited 60 heroin-addicted, predominantly male (77 percent) adults, aged 18 to 59 years, through advertising in local newspapers and word of mouth in New York City and Philadelphia. To be eligible, patients could not be addicted to any drugs other than heroin, caffeine, or nicotine. After initial heroin detoxification, the investigators randomly assigned participants to receive low-dose depot naltrexone, high-dose depot naltrexone, or placebo at the beginning of weeks 1 and 5. All participants received twice-weekly relapse prevention behavioral therapy.

After 8 weeks, 68 percent of the patients receiving 384 mg of naltrexone remained in treatment, compared to 60 percent of those receiving 192 mg, and 39 percent of those on placebo. The percentage of urine samples negative for opioids was highest for the group receiving 384 mg of naltrexone (62 percent) and lowest for the placebo group (25 percent). After receiving the medication, patients in the naltrexone groups reported "needing heroin" significantly less than those taking placebo.

The study participants experienced no apparent serious

NALTREXONE HELPS PATIENTS STAY IN TREATMENT More patients receiving 384 mg of depot naltrexone attended each weekly treatment session, compared with those receiving a smaller dosage of depot naltrexone or those who received placebo.



side effects. Despite previous reports associating high doses of naltrexone with hepatotoxicity, only one patient developed elevated liver enzymes, which the researchers attributed to a new-onset hepatitis C infection rather than the medication. Heroin overdose, another potential concern for patients on naltrexone, was not observed in the study; several patients did abuse heroin while on naltrexone, but reported no pleasure from it.

Encouraged by their results, Dr. Comer and her colleagues are beginning a 6-month trial with a larger number of participants. "We want to make sure the depot formula helps over a longer period of time," she explains. "Having more tools is really helpful for providers. Some people do better on methadone, others on naltrexone. We'll have more success if we can offer both."

Dr. Richard Hawks of NIDA's Division of Pharmacotherapies and Medical Consequences of Drug Abuse, says pharmaceutical companies are developing even longeracting versions of naltrexone—a 6-month sustained-release formula. "But a drug alone never works," he says.

“To be effective, the medication must be combined with behavioral therapy. Many years of behavioral therapy research shows that the longer someone is in treatment, the longer the time to relapse. Longer-acting, sustained-release medications help maximize this effect.”

Source

- Comer, Sandra D., et al. Injectable, sustained-release naltrexone for the treatment of opioid dependence. *Archives of General Psychiatry* 63(2):210-218, 2006.
NN

Interim Methadone Raises Odds of Enrolling in Comprehensive Treatment

Patients reduced heroin abuse and criminal activity while awaiting admission to a treatment program.

By Sarah Teagle, *NIDA NOTES* Contributing Writer

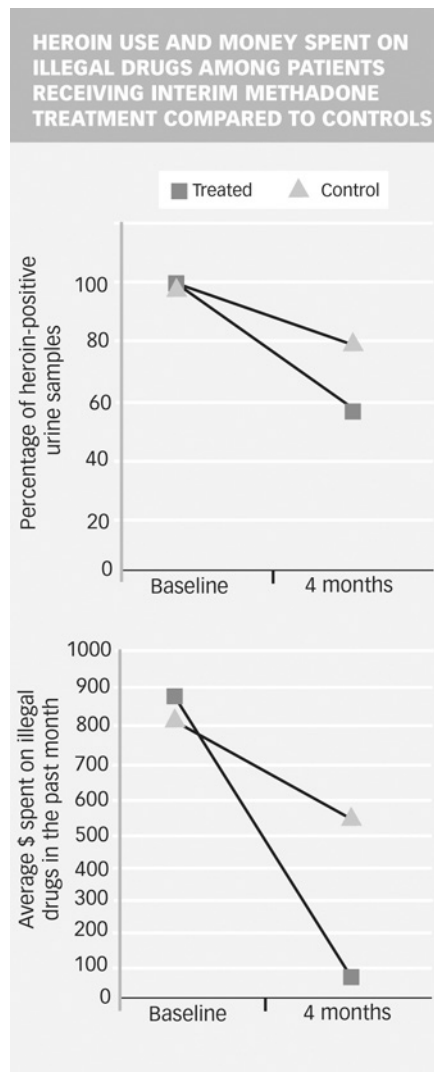
Providing methadone maintenance to heroin addicts while they are wait-listed for a treatment program can increase the likelihood they will enroll when spaces open up, say NIDA-funded researchers. The finding corroborates several previous studies in Europe and the United States. In the new study, participants who received methadone maintenance reported reduced use and criminal activity.

Across the Nation, full-to-capacity opioid treatment programs commonly put heroin-addicted men and women who present for treatment on waiting lists. By the time a treatment slot becomes available, the deferred applicants often have lost touch with the program or no longer desire treatment. The underlying idea of interim methadone maintenance is to capitalize on individuals' possibly transient motivation by providing help when help is requested, explains Dr. Robert Schwartz, who conducted the study with colleagues from the Friends Research Institute, the University of Maryland, and The Johns Hopkins University.

Benefits Early and Late

The researchers recruited 319 heroin-addicted men and women who placed themselves on the wait list of a single community-based program for methadone maintenance. The men and women typified people on methadone wait lists in the Baltimore area, in that most were African-American and reported abusing heroin daily as well as cocaine during the past month. The investigators randomly assigned each individual to receive free interim methadone maintenance for up to 120 days—the maximum time programs can legally provide methadone to an unenrolled individual—or to remain on a wait list. Both groups received information on how to access the waiting lists of the 11 other public methadone programs in the area.

The investigators interviewed each participant at the start of the study; upon his entry into comprehensive methadone treatment or, if he or she did not go into treatment, after 120 days; and 6 months after the second interview. Participants reported their alcohol, heroin, and cocaine abuse and provided urine samples at all three time points; those in the interim treatment group also provided samples at weeks 6 and 7 post-entry.



The results showed that 76 percent of study participants receiving interim methadone entered comprehensive care within 4 months, compared with only 21 percent in the control group. At the time of the last interview, 78 percent of interim methadone patients had entered a full-service program, compared with 33 percent of controls. Of the study participants who entered comprehensive treatment programs, 80 percent of those who had received interim methadone and 64 percent of controls were still attending at their last interviews.

The men and women who received interim treatment reported abusing heroin on a mean of 4 of the last 30 days prior to the 4-month followup interview, compared with 26 days for wait-listed patients. At the end of 4 months, the interim methadone group had a 57 percent rate of heroin-positive urine samples, while the control group had a 79 percent positive rate (see chart). The substantial difference in opiate-positive drug tests remained at the last interview, with a 48 percent positive rate among interim-

Study Specifics

Participants assigned to interim methadone began receiving the medication on their second day in the study, after completing an initial one-on-one orientation and physical exam. Nursing staff administered a dose of 20 mg, which increased by 5 mg per day with a target of 80 mg. Participants could slow or stop the dose schedule by seeing a nurse; they could exceed the 80 mg target by meeting with the program's emergency counselor. The only other service provided was emergency counseling, and three interim participants requested and received emergency counseling during the 4 months of treatment. Patients who failed to show up for three consecutive doses were discharged from the interim methadone—a program-wide rule that did not change for study participants. The clinic staff did not contact individuals who missed doses.

dramatically, to an average of \$76, compared with \$560 among the controls—a difference that was also maintained at the 6-month followup. “If we can corroborate this self-report data from other sources, the money saved from not spending on drugs would more than pay for the interim medication,” Dr. Schwartz notes. “It costs about \$20 to \$30 per week per person. That is cheap, especially when you consider the cost of criminal activity foregone, and the hospitalizations and incarcerations avoided.”

While more of the participants who received methadone entered full-service treatment, they took longer to do so

treated patients, compared to a 72 percent positive rate among controls. Participants who received interim methadone reported spending less money on drugs and receiving less illegal income in the past month compared with controls. On average, study participants reported spending \$872 monthly on illegal drugs at the beginning of the study. By the end, the methadone-maintained participants had reduced these expenditures

(a mean of 117 days) compared to those in the control group (59 days). However, Dr. Schwartz says, “People in the interim group knew they were going to get full service at the clinic where they were receiving their interim medication at the end of the study. Those in the control group who accessed treatment probably represent a higher-motivated subgroup—they actively sought it out using the local program information we gave them.”

Dr. Thomas Hilton of NIDA's Division of Epidemiology, Services and Prevention Research says, “Dr. Schwartz and his team have demonstrated that interim medication is a significant recruitment tool. This might even be an appropriate way to start treatment for everyone needing methadone maintenance. It exposes patients to some degree of structure, helps them ease into a more intensive, full-service program and accommodate their lifestyle to the structure required in the full service program.” Interim methadone also may be an important tool for retention, says Dr. Hilton, because patients may be ready for the medication before they're ready for counseling. After a few months on methadone alone, patients may be better able to engage with a counselor, making the relationship more productive. Six methadone programs in the Baltimore area have taken their cue from the study's findings and now offer interim maintenance. “What the interim treatment approach does is add patients to existing programs,” Dr. Schwartz explains. “It is not hard for the staff to do, it's less expensive, and it's effective. We hope it becomes more widespread.”

Sources

- Schwartz, R.P., et al. A randomized controlled trial of interim methadone maintenance. *Archives of General Psychiatry* 63(1):102-109, 2006.
- Schwartz, R.P., et al. A randomized controlled trial of interim methadone maintenance: 10-month followup. *Drug and Alcohol Dependence* 86(1):30-36, 2007. **NN**

Incentives Reduce Stimulant Abuse During Methadone Maintenance

Methadone maintenance patients who earned chances to win prizes by providing stimulant-negative urine samples were twice as likely as those who received usual care to attain abstinence from these drugs in a study conducted at six outpatient programs. Dr. Maxine Stitzer and colleagues in the NIDA Clinical Trials Network found that adding an abstinence-based incentive to usual care—daily methadone and individual and group counseling at least once a month—tripled the likelihood of continuous stimulant abstinence for 4 or more weeks during the 12-week study. Prizes for the incentive program cost about \$120 for each of the 388 participants, on average, or \$1.42 a day. Prize-based incentives have proven successful in helping stimulant abusers attain abstinence during community-based treatment (see “Low-Cost Incentives Improve Outcomes in Stimulant Abuse Treatment,” *NIDA NOTES*, Vol. 21, No. 1), and the new findings demonstrate the intervention’s efficacy for a diverse population of opioid-addicted patients receiving usual care in typical treatment settings.

Source

- *Archives of General Psychiatry* 63(2):201-208, 2006. **NN**

Naltrexone-Nicotine Patch Combination Shows Promise



Supplementing nicotine replacement therapy with naltrexone yielded improvements in outcomes in a double-blind 6-week trial. Among the 295 enrollees who completed the trial, quit rates were 72 percent with 100 mg of naltrexone, 51 percent with 25 mg, 48 percent with 50 mg, and 48 percent with a naltrexone placebo. Patients who took the 100 mg dose reported the greatest reductions in nicotine cravings and withdrawal symptoms. The investigators observed that patients receiving the 25 mg and 50 mg doses gained the least weight, and suggested that combination therapy with low-dose naltrexone and the patch be considered for smokers concerned about weight gain. The researchers cautioned that naltrexone augmentation for smoking cessation requires further study, as abstinence differences evened out by a 3-month followup, and did not recur at 6- and 12-month followups.

Source

- *Archives of Internal Medicine* 166(6):667-674, 2006. **NN**

Cocaine Abusers' Pretreatment Cue Responses Predict Recovery Success

In the future, patients' brain scans may help clinicians tailor addiction treatment to improve therapeutic outcomes.

By Lori Whitten, *NIDA NOTES* Staff Writer

A recent NIDA study strengthens prospects that brain imaging may one day help clinicians assign individual patients to treatment models that maximize their personal chances of a successful outcome. The study, conducted by Dr. Thomas Kosten and colleagues at Yale University School of Medicine, the University of Arkansas for Medical Sciences, and the Massachusetts Institute of Technology, correlated cocaine-addicted patients' regional brain responses to drug cues with their outcomes in subsequent treatment. The patients whose brain scans revealed rapid and strong activation in sensory, motor, and cognition- and emotion-processing brain areas were more likely to drop out of treatment and fail to achieve stable abstinence.

"A test that predicts treatment outcomes, especially vulnerability to relapse, could help guide individualized treatment. For example, a clinician might recommend an

extended stay in residential treatment or more intense behavioral intervention for patients with a propensity for relapse," says Dr. Kosten, now at Baylor College of Medicine.

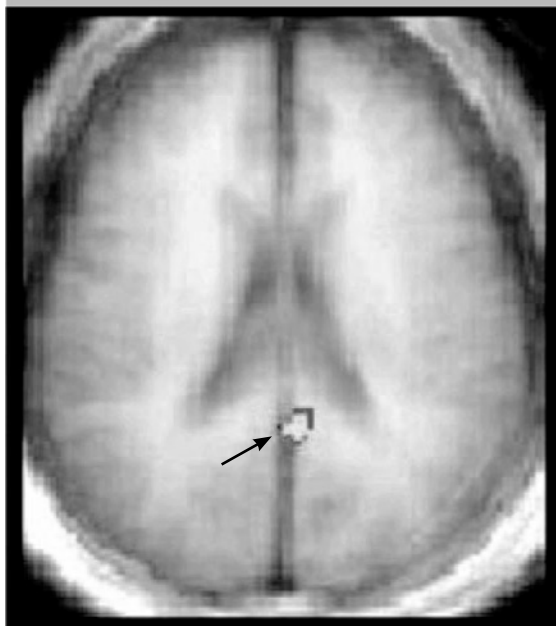
Dr. Kosten and colleagues pursued the implications of an intriguing finding made in a prior study of cocaine cue responses: In some patients, strong, rapid activation of brain areas associated with emotion and sensing preceded the onset of craving. Although craving itself does not generally predict relapse, Dr. Kosten's team speculated that cue-induced brain activation that occurs quickly and reflexively, below awareness, might do so. They hypothesized that patients who showed such responses during the first 30 seconds of cue exposure would also demonstrate poorer treatment outcomes.

To test their hypothesis, the investigators recruited 17 men and women who were participating in a trial of an antidepressant—sertraline—that is being evaluated as a possible treatment for cocaine addiction. The participants reported abusing cocaine 20 days, on average, during the month before the study. All met standard clinical criteria for cocaine addiction and had abused the drug for 6 years, on average. Most were new to treatment.

After being cocaine-free for 5 days, on average, each participant underwent functional magnetic resonance imaging (fMRI) while watching two 4-minute videotapes. The first minute of each tape reported on vegetable prices, and the participants' brain activity while hearing this emotionally neutral information served as a baseline for comparison. During the last 3 minutes, an actor pretended to smoke cocaine and experience a "rush." Immediately after viewing the tapes, each participant rated peak cocaine craving intensity on a scale from 0 to 10. After the imaging session, participants began taking either sertraline or a placebo daily and completed 2 weeks of residential treatment. During the 10-week outpatient phase of the trial, they were to continue their medication regimen, receive weekly individual cognitive-behavioral therapy, and submit urine samples three times a week.

fMRI TRACKS CUE-INDUCED BRAIN ACTIVITY

When cocaine-addicted patients watched a drug-related videotape, activation of the posterior cingulate cortex (highlighted in the brain image) occurred more quickly in those who subsequently relapsed.



WHAT RESEARCHERS KNOW ABOUT THE CINGULATE CORTEX AND BEHAVIOR

The cingulate cortex connects to both the limbic systems (emotion and motivation) and the prefrontal cortex (planning and control of behavior) and seems to integrate emotion and cognition. The anterior and posterior regions of the cingulate are connected to different brain areas and differ functionally.

Anterior Cingulate Cortex (ACC)	Posterior Cingulate Cortex (PCC)
Paying attention—The ACC monitors inputs from the senses (competing options) and selects what we attend to.	Responding reflexively—The PCC integrates sensory and movement information with established behavior patterns and acts “below awareness.” The PCC responds to reward and positive feedback.
Making decisions—Influenced by past experience, the ACC assesses risk, reward, and conflict. It works with areas of the frontal cortex to select a response.	Reacting emotionally—The PCC processes emotion-related autobiographical memories and the emotional perspective of self and others. Its activity correlates with internal physiological responses (heart rate, anxiety, and arousal level).
Inhibiting responses—The ACC integrates input from the prefrontal cortex and detects and corrects errors in behavior.	
Detecting and controlling emotions—The ACC monitors what is going on inside (feelings, pain, and bodily arousal) and controls voluntary suppression of these sensations.	

Interplay Within Cingulate Cortex?

Nine of the 17 participants relapsed, defined by the investigators as submitting fewer than 15 of a possible 30 cocaine-free samples during the study and not completing outpatient treatment. Participants taking sertraline were just as likely as those taking the placebo to relapse. Relapsers and nonrelapsers reported cue-induced cravings of comparable intensity. The two groups differed, however, on brain activation during the first 30 seconds of the cocaine-cue videotapes. Relapsers showed greater cue-induced activation than nonrelapsers in several areas of the cortex: the left precentral (movement control), right superior temporal (auditory processing), right lingual and right inferior occipital (visual processing), and the left posterior cingulate cortices. The cingulate cortex is integral to attention, response inhibition, emotional regulation, and decisionmaking (see chart).

The relapsers’ greater activation of the posterior cingulate cortex (PCC) was the most notable of the findings. Also significant was the lack of any difference between the outcome groups in activation of the neighboring anterior cingulate cortex (ACC). This contrasts with findings from previous studies, in which ACC activation and craving were associated in patients who had longer abstinence (average 14-28 days) and were imaged for periods longer than 30 seconds after being shown cues.

“If researchers can determine changes in brain activity that predict responses to particular treatments, then clinicians could match therapy with individuals’ scan results or even monitor progress in therapy.”

Taken together Dr. Kosten says, these results suggest that an interplay occurs between the PCC and ACC following exposure to cocaine cues and changes with increasing stability of abstinence. In patients highly vulnerable to cues, intense PCC activation occurs within 30 seconds of cue exposure and is positively associated with risk for relapse. In less vulnerable patients, early PCC activation is less intense, and these patients are able to activate the ACC to counter the association with relapse risk.

Dr. Kosten’s findings highlight the promise of imaging linked to behavioral assessments as a tool for guiding the treatment of addictions and other psychiatric disorders. They parallel a previous NIDA-funded study in which brain activity patterns during a decisionmaking task predicted treatment

outcomes among patients addicted to methamphetamine (see “Brain Activity Patterns Signal Risk of Relapse to Methamphetamine,” *NIDA NOTES*, Vol. 20, No. 5).

“If researchers can determine changes in brain activity that predict responses to particular treatments, then clinicians could match therapy with individuals’ scan results or even monitor progress in therapy,” says Dr. Kosten. More generally, studies that examine biological and behavioral predictors of treatment response elucidate the physiology underlying addiction—particularly the neural circuitry integrating stress, craving, and the propensity to relapse. New tools—for example, scanners that highlight brain areas that are working together—are expected to reveal more about these physiological processes. “With such functional connectivity imaging, one could examine how the anterior and posterior cingulate ‘talk’ to each other during a drug cue or other experience,” says Dr. Rajita Sinha, an investigator in the Kosten study.

“Eventually, researchers will integrate the findings of such studies into a complete picture that will specify therapeutic pathways or help in the development of targeted medications to reduce relapse probability,” adds Dr. Harold Gordon of NIDA’s Division of Clinical Neuroscience and Behavioral Research.

Source

- Kosten, T.R., et al. Cue-induced brain activity changes and relapse in cocaine-dependent patients. *Neuropsychopharmacology* 31(3):644-650, 2006. **NN**

Stress Cues Also Signal Relapse Risk

Exposing patients to stress cues at the beginning of cocaine addiction treatment triggers craving and measurable biological responses that may predict drug abuse outcomes during early recovery. NIDA-funded researchers found that stress-induced craving was associated with a shortened interval to relapse following inpatient treatment, while hormonal responses to stress predicted the amount of cocaine the patients consumed during relapse.

The findings were reported in a followup to prior research conducted by Dr. Rajita Sinha and colleagues at Yale University School of Medicine. In the previous study, patients who listened to tapes reminding them of a stressful experience and a drug-related experience demonstrated an elevated biological stress response and increased cocaine craving compared with their response to tapes of relaxing experiences (see "Cocaine-Related Environmental Cues Elicit Physiological Stress Responses," *NIDA Notes*, Vol. 20, No. 1).

Dr. Sinha and colleagues followed up with 49 of the 54 patients 3 months after completion of inpatient behavioral treatment. They found that patients who had experienced more intense cocaine craving while revisiting their stressful experiences via audiotape tended to relapse sooner. The probability of relapse 3 months after treatment was 56 percent among patients who reported no craving. Each unit increase on a craving intensity scale of 0 to 10 was associated with a 31 percent rise in the likelihood of relapse during the followup period.

Participants who released high levels of the stress hormones adrenocorticotrophic hormone (ACTH) and cortisol in response to the stressful tapes consumed more cocaine than low-level responders during the followup. Three months after treatment, high-level responders had consumed about 8 g of cocaine cumulatively over their cocaine abuse periods, while low-level responders consumed about 3 g.

The findings of the study suggest that different components of the stress response are associated with various aspects of relapse: craving with reinitiating abuse and hormonal responses with the ability to control intake after reinitiating abuse. "Greater

hormonal release during stress may 'prime' higher cocaine consumption or bingeing after return to abuse, perhaps by altering the rewarding effects of the drug," Dr. Sinha says.

Dr. Sinha and colleagues did not find a link between drug cue-induced craving and relapse outcomes, a result that is consistent with previous studies. However, because the drug cue imagery produced physiological reactions similar to those triggered by the stress cues, the researchers speculated that studies using a larger sample or exposure to actual drug cues, rather than just images of them, may show such an association.

Prior studies that did not find a link between cue-induced craving and relapse generally assessed only one or two dimensions of craving, Dr. Sinha points out. Studies that address multiple components—wanting the drug, feelings about the drug and about wanting it, drug-seeking behaviors, coping reactions, physiological arousal, and stress hormone levels—may better indicate vulnerability to relapse, she says.

"For people who are not addicted, knowing that you want a particular thing probably defines craving. Our findings suggest that for addicted people, craving is a 'state'—a multidimensional experience—comprised, in part, of stress-like arousal. In this state, desire becomes pathological, and people cannot delay gratification or divert their attention," says Dr. Sinha.

The results of Dr. Sinha's study suggest that stress-induced drug craving and physiological responses may be used as a diagnostic indicator of relapse propensity and might one day help clinicians tailor their interventions toward regulating stress and coping with stress-induced craving. "Research on each component and the role that it plays in continued drug abuse is just beginning, but such studies ultimately may improve our ability to help people attain long-term recovery," she says. ■

SOURCE

Sinha, R., et al. Stress-induced cocaine craving and hypothalamic-pituitary-adrenal responses are predictive of cocaine relapse outcomes. *Archives of General Psychiatry* 63(3):324-331, 2006.

NIDA's division of Basic Neuroscience and Behavioral Research

How Drug Abuse Affects the Brain and Alters Behavior Are Key Questions Driving Division's Work

By Debra P. Davis, *NIDA NOTES* Staff Writer

A compound that appears promising for treating cocaine relapse is wending its way along a chain of discovery and trial that links NIDA's various Divisions. Its discovery occurred under a grant from the Division of Basic Neuroscience and Behavioral Research (DBNBR), NIDA's locus for studies into the fundamental brain mechanisms underlying drug abuse and addiction.

Dr. David Shurtleff, director of the Division, sees his unit as the base of a pyramid upon which other NIDA Divisions and the scientific community at large build. "Much NIDA-supported research hinges on a basic understanding of the important biological components of drug abuse and addiction and how we can modify them to treat this disease," says Dr. Shurtleff. "Our research in DBNBR, which probes the genetic, molecular, neurobiological, and behavioral levels, is fed to all other Divisions at NIDA for further studies and for development of medications and new behavioral treatments."

With an eye toward developing a new medication for treating cocaine relapse, DBNBR "handed over" the JDTic compound, a potent and selective kappa-opioid antagonist that has been shown to significantly reduce stress-induced cocaine relapse in rodents, to the Division of Pharmacotherapies and Medical Consequences of Drug Abuse for further tests in animals and—if warranted—in people. Ultimately, the compound may undergo large-scale clinical trials sponsored by NIDA's Clinical Trials Network.

The flow of research is two-way: As DBNBR feeds the findings of its grantees to other Divisions, it also relies on them for information that drives the development of its own research portfolio. For example, says Dr. Shurtleff, "The Division of Epidemiology, Services and Prevention Research tells DBNBR what the trends in drug abuse are and who is affected."

Key Research Components

DBNBR's research portfolio is divided among four Branches: Genetics and Molecular Neurobiology, headed by Dr. Jonathan Pollock; Behavioral and Cognitive Science, under Dr. Minda Lynch; Chemistry and Physiological Systems, under Dr. Rao Rapaka; and Functional Neuroscience, run by Dr. Nancy Pilotte. Investigations fall into the following categories:

- Genetic, which seeks to pinpoint genetic variations that make some individuals more susceptible to addiction;
- Developmental, which examines, primarily in animal models, the effects of drugs on prenatal development as well as on the still developing brains of children and adolescents;
- Behavioral, which looks at the consequences of drug abuse on behavior and cognition, providing important information for the design of treatment and prevention interventions; and
- Neurobiological, which delves into the processes and mechanisms in the brain and nervous system underlying addiction.

SEA OF NEURONS This image appears on the Division's NIDA publications and posters.



The research projects touch on a broad range of drugs, health problems, populations, and scientific disciplines. For example, teams of scientists specializing in virology, immunology, neuroscience, and other disciplines are trying to determine how and why some individuals with HIV/AIDS develop a type of dementia called neuroAIDS and how exposure to neurotoxic drugs such as methamphetamine exacerbates this condition. Another study, by NIDA-supported scientists using technology developed by the California-based pharmacogenetics company Perlegen, Inc., is probing how genes affect tobacco addiction. The goal is to lay the groundwork for developing antismoking medications tailored to individuals who are genetically predisposed to nicotine addiction. Other nicotine studies focus on the effects of this drug on adolescents. Research by Dr. James Belluzzi and others shows that adolescent rats are more sensitive than adult rats to nicotine and that a combination of nicotine and acetaldehyde, another ingredient of cigarettes, is particularly addictive to the adolescents (see “Study Points to Acetaldehyde-Nicotine Combination in Adolescent Addiction,” *NIDA NOTES*, Vol. 20, No. 3).

A number of studies are examining how drug abuse changes the brain’s structure. They include research by Dr. Eric Nestler and colleagues looking at short- and long-term changes that cocaine engenders in the brain’s limbic system and studies by Drs. Terry Robinson and Bryan Kolb indicating that repeated exposure to amphetamine and cocaine alters neuronal structures called dendrites, which, in turn, increases sensitivity to the drugs.

“Thanks to advances in neuroscience and genetics, we’re finding answers to longstanding questions,” Dr. Shurtleff notes. “Now we’re able to view the human brain in action and understand how drug abuse affects the molecular mechanisms of cell signaling. As a result, we can develop new medications to stave off or reverse those effects. Information provided by the mapping of the mouse and human genomes is also helping us to answer longstanding questions about the etiology of drug addiction.” **NN**

Medical Care During Addiction Treatment Reduces Hospital Use



On-site delivery of primary care reduces emergency department (ED) visits and inpatient hospital stays over the next 12 months among adult patients in methadone maintenance or in long-term residential treatment programs, according to a recent article by Dr. Peter D. Friedmann and colleagues. Their longitudinal analysis showed that offsite referrals reduced hospitalizations, but not ED visits, among those in long-term residential programs. Neither on-site care nor offsite referral curbed health service use by outpatients in nonmethadone treatment programs. In all three types of programs, health care use declined after substance abuse treatment. Overall, ED visits decreased from 47 percent to 23 percent, and hospitalizations from 42 percent

to 13 percent; the greatest reductions were observed among patients with the longest stays in treatment. The National Treatment Improvement Evaluation Study included six methadone maintenance programs, 14 long-term residential programs, and 24 outpatient nonmethadone programs with over 2,000 patients. The investigators advocate future studies of the cost-effectiveness of integrating primary care into addiction treatment.

Source

- *Medical Care* 44(1):8-15, 2006. **NN**

Low-Cost Incentives Improve Outcomes in Stimulant Abuse Treatment

In community-based treatment programs, the intervention added \$2.42 per patient per day to counseling costs.

By Lori Whitten, *NIDA NOTES* Staff Writer

The opportunity to win rewards worth as little as \$1 for abstinence can help motivate outpatients to stay in behavioral therapy and remain drug-free, according to a NIDA Clinical Trials Network (CTN) study. At eight community-based addiction treatment programs across the United States, stimulant abusers who could earn a chance to win a prize by providing drug-free urine samples were four times as likely as peers who were not offered this incentive to attain 12 weeks of continuous abstinence. Prizes for the incentive intervention cost the programs about \$200, or \$2.42 a day per participant.

Many addiction treatment clinics face the challenge of high patient dropout rates. Reinforcing abstinence helps keep patients interested in attending treatment for longer periods, which can facilitate behavioral changes to keep them off drugs for the long haul," says Dr. Nancy Petry of the University of Connecticut School of Medicine, coleader of the study. Prior research has found that, no matter how it is achieved, duration of abstinence during treatment is one of the best predictors of abstinence 1 year later. "More patients achieve this therapeutic milestone with a boost from incentive programs," says the study's other coleader, Dr. Maxine Stitzer of The Johns Hopkins University School of Medicine.

The CTN investigators randomly assigned 415 treatment-seeking stimulant abusers (see chart) to one of two conditions: usual care or usual care plus abstinence-based incentives for 12 weeks. Usual care typically consisted of group counseling, although some patients received individual and family therapy. Patients gave urine and breath samples twice weekly. Research assistants tested the urine samples for stimulants, opiates, and marijuana, and tested the breath samples for alcohol.

Each participant in the incentive condition received immediate feedback on his or her samples. After submitting stimulant- and alcohol-negative samples, the patient could draw from an opaque container with 500 chips, each with words of encouragement or an assigned value: Half of the chips simply said, "good job;" 209 could be traded for \$1 prizes, 40 for \$20 prizes, and 1 for a \$100 prize. Prizes were conferred immediately and included many options, ranging from toiletries, snacks, and bus

CHARACTERISTICS OF STUDY PARTICIPANTS

Patients at eight community-based clinics across the country were ethnically diverse and generally reflected the national population of treatment-seeking stimulant abusers.

Characteristic	%
Ethnicity	
White	42
African-American	35
Hispanic	12
Other	9
Male	44
Unemployed	65
On parole or probation	35
Abuse of other drugs	
Alcohol	42
Marijuana	20
Opioids	9

tokens to kitchen items, telephones, and retail store certificates for televisions, music players, and DVD players. The number of draws earned increased by one each week in which all the

patient's samples were stimulant- and alcohol-negative, but fell back to one following a positive sample or an unexcused absence. When a participant first achieved two consecutive weeks of abstinence, he or she received a \$20 prize. Participants who submitted stimulant- and alcohol-negative samples could earn two bonus draws a week if their urine samples were also opioid- and marijuana-negative.

More patients in the incentive program (49 percent) than in usual care (35 percent) completed 12 weeks of counseling. Patients in the incentive group achieved an average duration of sustained abstinence of 4.4 consecutive weeks, compared with only 2.6 weeks among counseling-only patients. Nineteen percent of patients receiving the incentive intervention attained 12 weeks of continuous abstinence compared with 5 percent of those in usual care. Intervention patients also attended more counseling sessions (19 versus 16) and submitted more stimulant-negative urine samples during treatment than patients in usual care (48 versus 36 percent).

Incentives Accentuate The Positive

"Incentive programs, including low-cost ones, add excitement and additional reasons to attend substance abuse treatment. Many substance abusers are ambivalent about

Blending Initiative Disseminates Information on Low-Cost Incentives

Clinicians and administrators who wish to learn more about using low-cost incentives to motivate patients to stay off drugs can get information through the Blending Initiative, a program established by NIDA and the Substance Abuse and Mental Health Services Administration to speed the adoption of scientific findings into drug abuse treatment. The Blending Initiative has developed an awareness program that disseminates practical information on low-cost incentive programs and a summary of research evidence that supports their use as an adjunct to addiction treatment.

A DVD/CD-ROM describes the principles underlying incentive programs, the range of behaviors that clinics can target, and findings from studies of the intervention with a variety of patient populations. In the video component, clinicians, patients, and managers describe their experiences with the use of low-cost incentives in Manhattan and Connecticut outpatient methadone treatment programs. Viewers observe a group of Connecticut clients participating in a prize draw and a panel of directors and clinical managers discussing implementation challenges, ways to overcome problems, and the reasons they think the low-cost incentive program is effective. The CD-ROM component includes a flexible PowerPoint presentation suited for executive briefings or a 3-hour workshop. The Blending Initiative expects to release the information package in fall 2006, and it will be posted on NIDA's Web site, www.drugabuse.gov and on the Addiction Technology Transfer Center (ATTC) Web site, www.nattc.org.

"We anticipate that the awareness campaign will leave the addiction treatment community wanting more, for example, Web-based training and workshops on how to implement low-cost incentive programs," says Ms. Lonnetta Albright, director of the Great Lakes ATTC and leader of the Promoting Awareness of Motivational Incentives Blending Team.

The 2006 Blending Initiative program, "Bridges to the Future," was held October 16 and 17, 2006 in Seattle, Washington (see www.sei2003.com/blendingseattle/topics.htm).

treatment, and rewards may help them stay involved in counseling," says Dr. Petry. Extending retention in treatment may prolong abstinence, in part, because it gives counselors more time to help patients re-engage in a drug-free lifestyle, says Dr. Stitzer. Helping patients sustain abstinence once they leave therapy is a challenge for all treatments, including incentive programs.

Some previous clinical trials of voucher-based incentive programs showed benefits of the treatment persisting for 1 to 2 years, but others found no added value over the long term compared with usual care. Further research will focus on followup with patients to determine the conditions under which incentive interventions, particularly as applied by community-based treatment programs, support extended abstinence.

Other relatively small, often single-site NIDA-funded clinical trials over the past 15 years have demonstrated

that motivational incentives are an effective adjunct to standard therapy for opiate-, marijuana-, alcohol-, and cocaine-addicted patients. Patients in most of those early studies always received vouchers exchangeable for goods or services, rather than chances to win prizes, for positive behaviors; costs typically ran to about \$1,000 per patient over 3 months, with the result that few community programs adopted the motivational incentive approach. Dr. Petry developed her prize-drawing system to make incentives affordable for community programs. She has tested it successfully in several Connecticut treatment programs, and now its effectiveness is confirmed by the CTN trial. NIDA is collaborating with the Substance Abuse and Mental Health Services Administration's Addiction Technology Transfer Center to promote awareness of the low-cost motivational incentive technique (see textbox).

The CTN researchers note that some community-based treatment providers resist the idea of motivational incentives based on a belief that clinicians should not reward patients for behaviors "that they are supposed to do anyway." In response, the researchers point out that groups and individuals often use external incentives to motivate others—from employees' bonuses to children's allowances for household chores. Dr. Stitzer advocates a shift in

perspective from punishing lapses to celebrating successes. She observes that counselors have often changed their views when they have seen incentives help revolving-door patients stay in therapy. "Incentive programs—the idea of catching people being good and rewarding the behavior—can infuse addiction treatment with a positive outlook and reinvigorate patients and counselors," says Dr. Stitzer.

Source

- Petry, N.M., et al. Effect of prize-based incentives on outcomes in stimulant abusers in outpatient psychosocial treatment programs: A National Drug Abuse Treatment Clinical Trials Network Study. *Archives of General Psychiatry* 62(10):1148-1156, 2005. **NN**

Study Finds Withdrawal No Easier With Ultrarapid Opiate Detox

Three serious adverse events among 35 ultrarapid procedures were all related to unreported preexisting medical conditions.

By Lori Whitten, *NIDA NOTES* Staff Writer

Heroin-addicted patients who undergo so-called ultrarapid, anesthesia-assisted detoxification suffer withdrawal symptoms as severe as those endured by patients in detoxification by traditional methods, according to a NIDA-funded clinical trial. Researchers Dr. Eric Collins and colleagues at the College of Physicians and Surgeons of Columbia University concluded that there is no compelling reason to use general anesthesia in the treatment of opiate dependence, especially as it presents particular safety concerns. The new findings corroborate those of three international studies.

The ultrarapid detox technique, developed about 15 years ago by clinicians who hoped to mitigate the discomfort of withdrawal and speed the initiation of relapse prevention therapy, relies on a general anesthetic to sedate the patient for several hours while an opiate blocker precipitates withdrawal. The method is not covered by insurance, which makes it difficult to determine how many patients have

received anesthesia-assisted detox.

To compare anesthesia-assisted detox with other approaches, Dr. Collins and colleagues enrolled 106 people seeking heroin detox at Columbia University Medical Center's Clinical Research Center. The patients, aged 21 through 50, had abused heroin every day during the past month. All spent 3 days as Center inpatients during detox, then were scheduled for twice-weekly outpatient relapse prevention psychotherapy and naltrexone maintenance (50 mg/day) for 12 weeks.

The investigators randomly assigned the participants to one of three detox methods (see chart). The goal of each method was to minimize patients' discomfort during withdrawal. In the ultrarapid approach, physicians put patients under anesthesia for 4 to 6 hours while administering naltrexone, a medication that precipitates withdrawal by blocking opioid molecules from their receptors in the brain. In the second method, patients remained awake

and took a single dose of buprenorphine, a medication that eases withdrawal symptoms by moderating and smoothing the rate of opioid clearance from the brain. In the third approach, patients also remained awake and received clonidine and other nonopioid medications as needed to counter symptoms for all 3 inpatient days. These

RESEARCHERS COMPARE THREE OPIATE DETOX METHODS Investigators studied the safety profile and withdrawal symptom control of three detoxification methods used in 106 patients at Columbia University Medical Center.

	Inpatient treatment				Outpatient treatment
	Day 0	Day 1	Day 2	Day 3	Day 4 through week 12
Anesthesia-Assisted		Anesthesia 4-6 h → 2 h monitoring in post-anesthesia unit → naltrexone induction (50 mg) Clonidine and nonopioid medications as needed for withdrawal symptoms	Begin naltrexone maintenance (50 mg/day) (continue through end of study) Ancillary withdrawal medications continued	Discharge from inpatient treatment Ancillary withdrawal medications continued	Twice-weekly psychotherapy Naltrexone maintenance medication (50 mg/day)
Buprenorphine-Assisted	Buprenorphine (8 mg)	Clonidine and nonopioid medications as needed for withdrawal symptoms	Naltrexone induction (12.5 mg) Ancillary withdrawal medications continued	Discharge from inpatient treatment Naltrexone induction continues (25 mg) Ancillary withdrawal medications continued	Twice-weekly psychotherapy Naltrexone maintenance medication (50 mg/day)
Clonidine-Assisted		Clonidine and nonopioid medications as needed for withdrawal symptoms	Ancillary withdrawal medications continued	Ancillary withdrawal medications continued Discharge from inpatient treatment	Twice-weekly psychotherapy Begin 2-day naltrexone induction on day 7 (12.5 mg, then 25 mg), followed by naltrexone maintenance starting on day 9 (50 mg/day)

medications were available to all groups as needed for the duration of the inpatient phase. Throughout detox, the researchers closely monitored patients for complications, assessed physical indications of withdrawal, and asked the participants to rate their subjective experiences.

Once awakened from anesthesia, patients in the ultrarapid detox group demonstrated and reported symptoms of discomfort comparable to those experienced by participants receiving the buprenorphine- and clonidine-assisted methods (see chart). Three patients receiving the anesthesia-assisted method experienced serious adverse events—pulmonary and psychiatric complications as well as a metabolic complication of diabetes, all of which required hospitalization. The complications were related to preexisting medical conditions that the patients had failed to reveal when they were screened for admission into the study. No adverse events occurred with the other detox methods.

Treatment outcomes among the three groups were similar. Following detox, the researchers offered all the patients relapse prevention therapy consisting of outpatient counseling and naltrexone, which counteracts the pleasurable effects of subsequently administered opioids. More than 90 percent of the patients who received the anesthesia- and buprenorphine-assisted detox completed naltrexone induction; only 21 percent of those receiving clonidine completed induction. By the third week, more than half the patients in all three groups had dropped out of the study;

only 18 percent remained in treatment the full 12 weeks. The percentages of patients submitting opiate-positive urine samples during outpatient treatment also were comparable, roughly 63 percent, across the three detox methods.

“No Advantage”

“Although providers advertise anesthesia-assisted detox as a fast and painless method to kick opiate addiction, the evidence does not support those statements,” says Dr. Collins. “Patients should consider the many risks associated with this approach, including fluid accumulation in the lungs, metabolic complications of diabetes, and a worsening of underlying bipolar illness, as well as other potentially serious adverse events,” he says. Those with preexisting medical conditions—including some psychiatric disorders, elevated blood sugar, insulin-dependent diabetes, prior pneumonias, hepatitis, heart disease, and AIDS—are particularly at risk for anesthesia-related adverse events. “Careful screening is essential with the anesthesia-assisted method, because the thought of sleeping through withdrawal is so compelling that some patients may conceal their medical histories,” says Dr. Collins.

“We now have several rigorous studies indicating that anesthesia-assisted detox—a costly and risky approach—offers no advantage over other methods,” says Dr. Ivan Montoya of NIDA’s Division of Pharmacotherapies and Medical Consequences of Drug Abuse. Dr. Montoya notes, “The low retention of patients in subsequent outpatient treatment in the present study, which is not unusual for the opiate-addicted population, highlights the need to engage people in long-term recovery after detoxification.” Naltrexone can help motivated patients stay off opiates, but many do not stick to the regimen of daily tablets because of the medication’s side effects of anxiety and restlessness. Long-acting monthly injections of naltrexone, which are now available for alcoholism treatment, may work better for patients and show promise in NIDA-supported clinical trials.

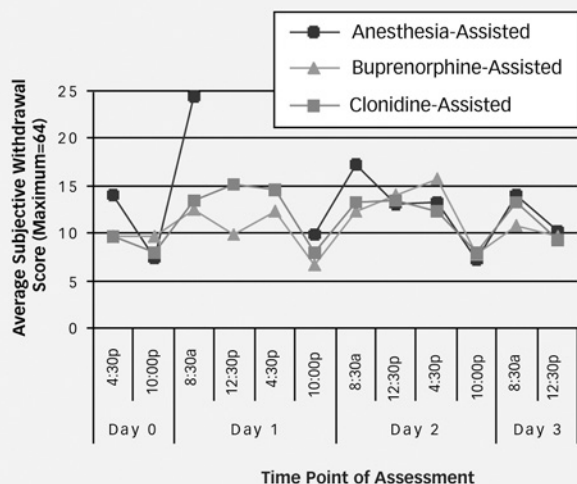
Dr. Montoya also points out that with the current epidemic of prescription painkiller abuse, clinicians need more research on cost-effective detox methods for these opiates (see “2003 Survey Reveals Increase in Prescription Drug Abuse, Sharp Drop in Abuse of Hallucinogens,” *NIDA NOTES*, Vol. 19, No. 4). Some clinics are using buprenorphine for this purpose, and NIDA-funded investigators are studying various methods to improve prescription opiate detox and help patients engage in longer term treatment.

Source

- Collins, E.D., et al. Anesthesia-assisted vs buprenorphine- or clonidine-assisted heroin detoxification and naltrexone induction: A randomized trial. *Journal of the American Medical Association* 294(8):903-913, 2005. **NN**

IN THREE DETOX METHODS, WITHDRAWAL SYMPTOM SEVERITY WAS SIMILAR

During a 72-hour inpatient detoxification stay, patients rated each of 16 withdrawal symptoms—for example, “I feel like vomiting,” “I have cramps in my stomach,” “I feel anxious,” and “My eyes are tearing”—on a scale from 0 (not at all) to 4 (extremely). Symptom severity generally did not differ between heroin-addicted patients receiving anesthesia-, buprenorphine-, or clonidine-assisted methods. Researchers did not assess withdrawal symptoms for the anesthesia-assisted group during general anesthesia and the immediate recovery period.



Buprenorphine Plus Behavioral Therapy Is Effective For Adolescents With Opioid Addiction

A new study looks at extending the role of buprenorphine for treatment of adolescents.

BY Patrick Zickler, *NIDA NOTES* Contributing Writer

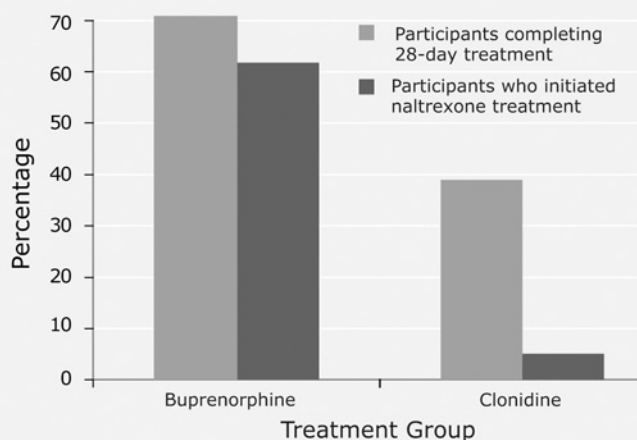
Adolescents addicted to opioids responded better to buprenorphine than clonidine in a clinical trial in which all patients also received behavioral therapy. In the NIDA-supported comparison trial at the University of Vermont, adolescents who received buprenorphine attended more scheduled counseling sessions than peers who received clonidine and had higher rates of successful induction to a relapse prevention regimen of naltrexone. The study, led by Dr. Lisa Marsch, is the first published randomized controlled study of treatments for adolescents addicted to opioids.

“Heroin abuse among American teens has doubled over the past decade, and abuse of prescription opioids such as OxyContin and Vicodin has increased even more,” says Dr. Marsch. “In light of those figures, it’s important to have a scientific basis for selecting treatments for opioid-dependent teens. We know from previous research and clinical experience that buprenorphine and, to a lesser extent, clonidine are among the medications that have been shown to be effective for treating opioid-addicted adults, but we haven’t known how helpful they can be for adolescents.”

Dr. Marsch and colleagues enrolled 36 opioid-addicted adolescents, aged 13 to 18, in a 28-day outpatient treatment program. Half the participants (9 male, 9 female) received buprenorphine in tablet form, the rest (5 male, 13 female) clonidine via transdermal patch; each patient also was given a placebo resembling the other treatment. Medication dosages varied depending on each participant’s weight and the amount of drug he or she reported abusing before beginning treatment; dosages of buprenorphine were in the low to moderate range of those typically given to opioid-addicted adults.

All participants also received behavioral therapy based on the Community Reinforcement Approach: three 1-hour sessions each week of counseling on methods to minimize involvement in situations that might lead to drug-taking, training to help recognize and control urges to abuse opioids, and encouragement to recruit family members as allies for abstinence. Participants earned vouchers worth \$2.50 for the first opioid-negative urine sample, plus an additional \$1.25 for each subsequent one, and a \$10

BUPRENORPHINE DETOXIFICATION SETS STAGE FOR RECOVERY Opioid-addicted adolescents who entered a detoxification program with buprenorphine were more likely than others receiving clonidine to maintain abstinence throughout a 28-day detoxification program and more likely to begin treatment with naltrexone after detoxification.



bonus for each set of three consecutive negative samples. Continuous abstinence could earn participants \$152.50 in vouchers redeemable for rewards such as ski passes, CDs, gym passes, and clothing.

Buprenorphine and clonidine both supported high rates of abstinence. Among participants who completed treatment, rates were 78 percent and 81 percent, respectively, confirmed by urine samples provided at the thrice-weekly sessions. However, nearly twice as many buprenorphine as clonidine recipients completed the 4-week treatment (72 percent compared with 39 percent). “The high rate of retention in the buprenorphine group is particularly noteworthy,” Dr. Marsch says, “because long-term success in recovery is directly related to the amount of time patients spend in treatment.” And, she adds, the willingness of most patients who received buprenorphine to continue treatment with naltrexone following completion of the 28-day program is similarly encouraging. Sixty-one percent of the buprenorphine group, but only 5 percent of those who received clonidine accepted naltrexone.

“Dr. Marsch’s research is an important first step in systematically studying adolescents who are addicted to opioids,” says Dr. Ivan Montoya of NIDA’s Division of Pharmacotherapies and Medical Consequences of Drug Abuse. “We know that there are differences in the patterns of opiate abuse and addiction in young people compared with adults. We need dedicated studies like this one to understand how teens are affected by opiate drugs and how best to treat them.”

The next step in Dr. Marsch’s research will involve a larger sample of young opioid abusers. “We want to

evaluate buprenorphine’s effectiveness if treatment is extended to 2 months rather than 28 days,” she says. “We will also examine the most effective doses and dosing regimens for various subgroups of young patients.”

Source

- Marsch, L.A., et al. Comparison of pharmacological treatments for opioid-dependent adolescents: A randomized controlled trial. *Archives of General Psychiatry* 62(10):1157-1164, 2005. **NN**

Court-Mandated Treatment Works as Well as Voluntary

Regardless of their impetus for participating in drug treatment—internal drive or external pressure—men had similar outcomes in the long term.

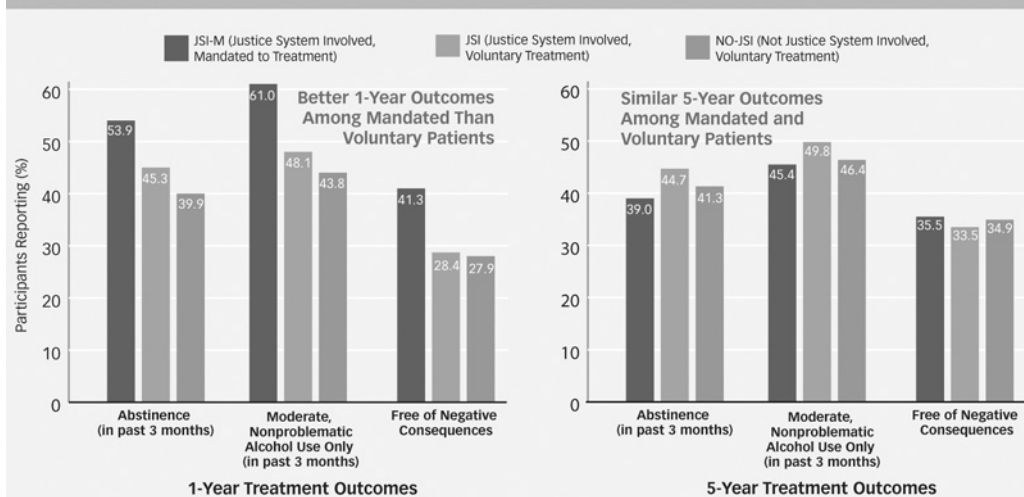
By Lori Whitten, *NIDA NOTES* Staff Writer

A group of men who completed court-ordered treatment for alcohol and drug problems reported lower intrinsic motivation at the beginning of treatment, but, 5 years later, reported the same rates of abstinence, employment, and rearrest as peers who sought help on their own. The findings from a NIDA- and Department of Veterans Affairs (VA) Health Services Research and Development Service-supported analysis of data on treatment outcomes affirm the results of shorter term studies that have shown similar therapeutic outcomes for voluntary and legally mandated patients. The new study also included an important, but largely unstudied, comparison group: people who had been in court, but were not mandated to enter treatment.

“Once in a therapeutic environment, mandated patients seem to reflect on their situation and accept the need for treatment,” says Dr. John Kelly, lead investigator of the study, conducted at the VA Palo Alto Healthcare System and Stanford University School of Medicine. “Our findings suggest that people can learn from the ‘teachable moment’ offered by a judicial mandate, even though the initial motivation for treatment is external. Judicial mandates may provide an opportunity for offenders to gain access to and benefit from needed treatment.”

Drs. Kelly, Rudolf Moos, and John Finney analyzed data, gathered by Drs. Moos and Finney and Dr. Paige Ouimette, on 2,095 men who were treated for alcohol and drug problems in 15 VA programs and followed for 5 years. About half the men (54 percent) were addicted to drugs; 80 percent were dependent on alcohol. Most (82 percent) had no criminal justice system involvement and entered treatment voluntarily (No-JSI); 7 percent were on probation or parole and were required to partici-

MANDATED TREATMENT WORKS Patients legally mandated to treatment reported better outcomes than nonmandated offenders and nonoffenders 1 year after residential treatment for alcohol and drug problems. Five-year outcomes were similar among the three groups.



pate in treatment by order of a court or criminal justice official (JSI-M); 11 percent had been before a court, but not mandated to treatment (JSI). About half (49 percent) of the participants were African-American; 45 percent were White; and the remaining 6 percent were Hispanic, Native American, or Asian. Most (74 percent) were unemployed when they started treatment.

The men completed 21 or 28 days of residential treatment, which took one of three therapeutic approaches: group psychotherapy and individual activities based on the 12-step approach, cognitive-behavioral therapy, or a mix of both. When they completed treatment, the men were urged to participate in outpatient programs and self-help activities.

At the beginning of treatment, each man completed a questionnaire that assessed characteristics considered important to recovery: motivation, self-efficacy, coping skills, 12-step participation, psychiatric symptoms, history of negative consequences of alcohol and drug problems, number of previous treatment episodes, and whether they considered themselves to be addicted. They also reported any prior year arrests and any judicial mandate for treatment. At the end of the treatment program, participants repeated the assessment and reported their perceptions

of the therapeutic experience. Most also received a self-administered assessment in the mail at the 1- and 5-year follow up points, with the rest contacted by telephone or in person. Research assistants telephoned patients when necessary to complete or clarify information.

In the initial assessment, men in the JSI-M group reported experiencing fewer negative consequences of alcohol and drug consumption, fewer symptoms of depression and anxiety, and less desire to abstain than No-JSI or JSI participants. Fewer mandated (45 percent) than voluntary patients (58 percent) met the standard clinical criteria for drug addiction. Voluntary patients more frequently recognized their addictions, connected them to other problems, and reported a readiness to change.

Rearrest Rates Fall, Remain Low

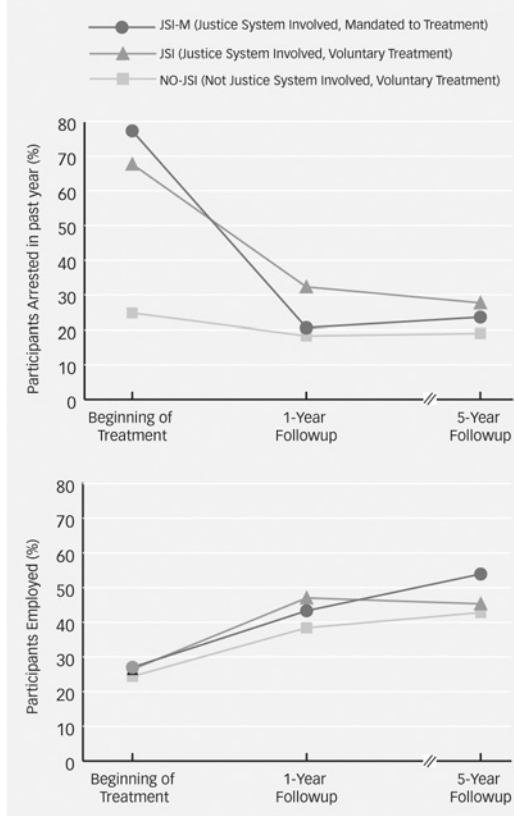
At the end of treatment, all three groups of patients demonstrated enhanced coping skills and expressed more confidence that they could resist alcohol or drugs in high-risk situations. Symptoms of psychological distress improved for participants in all groups. At the 1-year followup, larger proportions of JSI-M participants reported abstinence, successful moderation in their use of alcohol, and freedom from drug-related consequences (for example, missing work or fighting with a family member because of drugs) than JSI and No-JSI participants (see chart). Arrest rates for the two JSI groups fell dramatically after treatment. Mandated patients showed arrest rates similar to those of their No-JSI peers (about 20 percent) and lower than those of their JSI peers (32 percent) at the 1-year followup. Five years after treatment, most outcomes among the three groups did not differ (see chart).

The investigators believe that, in addition to the other positive effects of treatment, mandated patients may acquire motivation to change. "The high level of camaraderie in VA residential treatment, where these individuals interacted with self-motivated peers, may have contributed to a shift in attitude," says Dr. Kelly.

The implications of Dr. Kelly's findings go beyond the criminal justice population, says Dr. Beverly Pringle, formerly of NIDA's Division of Epidemiology, Services and Prevention Research. "The idea that patients must want to change seems to permeate current practice, but the drug abuse treatment field may need to reexamine its defini-

ARREST RATE FALLS, EMPLOYMENT RATE RISES AFTER TREATMENT

At the 1-year and 5-year followup, mandated patients showed arrest rates similar to those of nonmandated offenders and nonoffenders. Patients in all three groups demonstrated improved employment rates at followups.



tion of motivation," she says. Clinical measures of motivation mostly indicate intrinsic drive to change, but extrinsic motivators as well as rewards can increase treatment entry and improve long-term outcomes.

Source

- Kelly, J.F.; Finney, J.W.; and Moos, R. Substance use disorder patients who are mandated to treatment: Characteristics, treatment process, and 1- and 5-year outcomes. *Journal of Substance Abuse Treatment* 28(3):213-223, 2005. **NN**

Checkpoint System Catches Relapse Early and Facilitates Return to Treatment

Researchers in Chicago apply an old medical maxim: "Chronic diseases require chronic cures."

By Lori Whitten, *NIDA NOTES* Staff Writer

Supplementing regular recovery checkups with motivational interviewing and active linking to treatment can get relapsing patients back into treatment sooner and help them stay longer, report NIDA-funded researchers. In the 2 years following treatment, patients who received the additional interventions were three times as likely to reenter treatment as others who received assessments only.

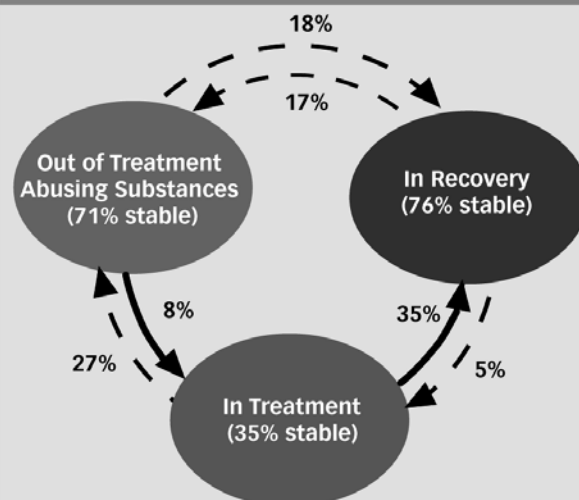
Lead investigator Dr. Christy Scott and coinvestigator Dr. Michael Dennis developed the effective intervention, which they call the Recovery Management Checkup (RMC) system, to expedite the recovery of people who had attended treatment and were now living in the community and experiencing substance abuse problems. They say the findings suggest that their approach to treating substance abuse as a chronic condition may help patients shake off the shame of relapse. "By the time patients had participated in checkups for 2 years, many who were initially reluctant to reenter treatment would call a peer to link them with help after a slip," says Dr. Scott, of Lighthouse Institute in Chicago, a Division of Chestnut Health Systems, Inc.

Intervention Matches Relapse Patterns

In developing the RMC system, the researchers built on previous studies in which they had identified patterns of chronic substance abuse, relapse, and recovery. They found that, during the first 3 years after treatment, people frequently transitioned between recovery, substance abuse, and treatment—a cyclic pattern suggesting that periodic checkups, with intervention when necessary, might help shorten relapse episodes. They also researched approaches used to manage other chronic health conditions and found that monitoring for relapse and reducing the time from relapse to treatment reentry improved long-term outcomes.

To implement the RMC system, Drs. Scott and Dennis hired and trained a cadre of research assistants and linkage managers, many of whom were local recovering individuals. Chestnut staff and clinical colleagues at Haymarket Center, the largest addiction treatment provider in Illinois, interviewed 448 men and women who had met the standard criteria for a substance abuse diagnosis at some time in their lives, had abused alcohol or other drugs

FOR MOST PATIENTS RECOVERY IS CYCLICAL, NOT LINEAR The researchers tracked the average percentages of patients moving between points in the recovery cycle—living in the community and abusing substances, in treatment, or in recovery—each quarter during the 2-year study. The goal of the Recovery Management Checkup system is to increase treatment reentry and recovery (movement along the solid arrows).



† "Stable" indicates that patients did not transition from one point to another in the cycle.

Reprinted from *Drug and Alcohol Dependence*, Vol. 78(3): 325-338, Scott, C.K.; Dennis, M.L.; and Foss, M.A.: "Utilizing recovery management checkups to shorten the cycle of relapse, treatment reentry, and recovery," © 2005, with permission from Elsevier.

in the past 90 days, were not in protective custody, and intended to live in Chicago for the next year. Cocaine, alcohol, opiates, and marijuana were the most commonly abused drugs. Immediately following the interview, patients received a referral to Haymarket Center for treatment—60 percent as residents and 40 percent as out-patients—for 27 days, on average; 11 percent remained in treatment for 90 days or more. Upon leaving treatment, each patient scheduled eight quarterly followup appointments. Before the first checkup, researchers randomly assigned the patients to either the RMC intervention or an assessment-only control group.

At each checkup appointment, patients met with a research assistant. The assistant administered a 45-minute version of the Global Appraisal of Individual Needs assessment and ascertained information about the patient's living

situation and substance involvement. If the patient had not abused any substance during the past 90 days, the assistant encouraged continued abstinence and scheduled the next appointment. Patients who reported slips were merely advised to reenter therapy if they were in the control group, but met with a linkage manager if they were in the intervention group and living in the community.

The linkage manager conducted motivational interviews, usually lasting less than 30 minutes, in which he or she provided feedback on patients' substance abuse and related problems, discussed ways to work through barriers to treatment reentry, and considered motivations to return to therapy. If a patient was willing to reenter treatment (even with low motivation), the linkage manager scheduled an appointment, telephoned with a reminder, and arranged transportation. The linkage manager provided assistance for 2 weeks, but afterward, responsibility for continuing therapy fell to the patient. Between RMC appointments, the patient received cards and calls from the research office; these served as a reminder of the next visit and carried a message of support from the research team.

Checkups Boost Check-Ins

The researchers were able to interview patients at both the beginning and end of a quarter in 87.5 percent of cases. They categorized each patient's current status as in the community abusing substances, in treatment, in recovery (no substance abuse, problems, or treatment while living in the community), or incarcerated. Between the beginning and end of each quarter, about one-third of the patients, on average, transitioned from one status to another. Most (82 percent) transitioned at least once during the study, with 62 percent moving between points several times (see chart on previous page).

Among patients who relapsed, 67 percent of RMC patients reentered treatment within 90 days after the checkup, compared with 51 percent of assessment-only patients. RMC patients returned to treatment sooner (27 versus 45 days) and stayed in treatment longer (7.75 versus 4.68 days), on average, than the control group. Length of treatment predicted transition to recovery at the next quarterly assessment—for every 10.5 days in treatment, a patient was 1.2 times more likely to be abstinent at the next quarterly checkup.

"The checkups help a patient evaluate his or her behavior and recovery-related issues—much as a person with diabetes would report on blood sugar levels and diet and exercise patterns," says Dr. Thomas Hilton of NIDA's Division of Epidemiology, Services and Prevention Research. "By employing individuals in recovery as linkage managers, the program also offered an opportunity for the patient to return to treatment or at least receive support from someone who has been there."

Drs. Scott and Dennis plan to tailor the checkups for specific populations—for example, women involved in the criminal justice system.

Source

- Scott, C.K.; Dennis, M.L.; and Foss, M.A. Utilizing recovery management checkups to shorten the cycle of relapse, treatment reentry, and recovery. *Drug and Alcohol Dependence* 78(3):325–338, 2005. **NN**

Medications Development Division Nurtures the Creation of New Addiction Treatments

By Lori Whitten, *NIDA NOTES* Staff Writer

In the Anti-Drug Abuse Act of 1988, Congress mandated NIDA to promote the development of medications “to treat the symptoms and disease of drug abuse.” Research by NIDA-supported scientists and others had by then made clear that drug abuse is a neurological disorder treatable by pharmacotherapy, but only three anti-addiction medications were available (disulfiram, methadone, and naltrexone), all developed in the 1960s and early 1970s. Congress recognized the need for Federal leadership and, because of NIDA’s resources and expertise, entrusted the Institute with facilitating the development of pharmacotherapies to treat addiction.

With an initial appropriation of \$8 million, NIDA launched a Medications Development Program that same year and formally established the Medications Development Division in 1990. From its beginning, the Division has supported and coordinated academic and private sector scientists engaged in every stage of medications development—from the creation of new compounds in the laboratory to the testing of products in clinical trials. The Division’s efforts have been instrumental in bringing buprenorphine and buprenorphine-naloxone—safe and effective treatments for opiate addiction, the latter suitable for office-based therapy—to the Nation’s clinics and pharmacy shelves. Among other current priorities, the Division supports work to establish the safety and efficacy of the smoking-cessation aids nicotine replacement and bupropion for people with psychiatric conditions, pregnant women, and adolescents.

Under the leadership of Division Director Dr. Frank Vocci, Dr. Nora Chiang, Chief of the Chemistry and Pharmaceutics Branch, manages laboratory research grants designed to develop new compounds with therapeutic potential; Dr. Jane Acri, Director of the Addiction Treatment Discovery Program, leads a multidisciplinary team that screens compounds and advances those with therapeutic potential into testing for safety and efficacy; and Dr. Ahmed Elkashef, Chief of the Clinical/Medical Branch, coordinates the evaluation of data from clinical trials.

The Division pursues a dual strategy that balances the need to advance scientific discovery and the need to find safe and effective treatments as rapidly as possible. On one track, NIDA intramural and funded scientists seek new medications. Researchers in the Cocaine Treatment

DUAL STRATEGY GUIDES NIDA’S DRUG ABUSE MEDICATION DEVELOPMENT

Test Existing Medications

Researchers evaluate marketed medications whose chemical properties suggest they might reduce drug abuse.

Characteristics

Medications are already approved for marketing for other conditions.

Known safety profile.

Less expensive to develop than new compounds.

Short time to gain approval for marketing.

Examples

Methadone and buprenorphine, widely used for opiate addiction treatment, were first used as analgesics.

Bupropion, prescribed for nicotine addiction, was first used for depression.

Currently being evaluated for cocaine abuse: modafinil (narcolepsy), topiramate (seizures), disulfiram (alcohol dependence), bupropion.

Currently being evaluated for cocaine and methamphetamine abuse: selegiline (Parkinson’s disease), baclofen (muscle spasms), ondansetron (prevents chemotherapy-related nausea).

Develop New Medications

Researchers investigate the therapeutic potential of new compounds.

Characteristics

Lengthy process of discovery. Relies on behavioral, biochemical, and neuroimaging experiments with ultimate translation of laboratory findings to clinical studies.

Takes advantage of breakthrough discoveries in neuroscience. Potential for discovering medications that affect multiple addictions.

Examples

Two compounds (GBR 12909, NS2359) that generate modest and long-lasting increases in dopamine have reached human safety evaluation. NIDA stopped testing of GBR 12909 because of cardiovascular concerns, but continues to evaluate NS2359.

A compound (CP-154,526) that blocks the neurochemical corticotropin-releasing factor 1 attenuates stress-induced relapse to cocaine and heroin in animals.

Discovery Program have identified and evaluated more than 3,000 compounds whose molecular characteristics or performance in animal studies suggested they might reduce cocaine craving and prevent relapse. This process has, for example, identified a new compound called JDTic, which has anti-stress and antidepressant characteristics and prevents relapse in animals, and is developing the agent for potential clinical testing. Under the second approach, NIDA has established a network of clinical investigators to screen marketed medications with neurochemical effects that suggest a potential for reducing drug abuse (see chart, page 4 of *NIDA NOTES*, Vol. 20, No. 6). Among 65 medications examined so far, eight potential treatments for cocaine abuse—including topiramate, disulfiram, and modafinil—have advanced to the confirmatory stage of clinical trials in cocaine-dependent patients.

Throughout the 1990s, as well, the Division advanced research on vaccines that prevent drugs from reaching the brain. A vaccine to prevent cocaine addiction and another for nicotine abuse are now being tested for safety and efficacy.

Because medication development is an enormously complex and costly enterprise, the Division collaborates with other Government agencies, particularly the U.S. Food and Drug Administration (FDA), and the pharmaceutical industry. The relationship with FDA has been vital to overcoming scientific and regulatory barriers to evaluating new medications for opiate addiction and shepherding buprenorphine through the necessary approvals. The Division's relationships with industry frequently have been formalized as Cooperative Research and Development Agreements (CRADAs). In this type of arrangement, NIDA provides expertise, equipment, and facilities to test a corporate-owned compound as a potential pharmacotherapy; if the results are as hoped and a marketable medication results, the company maintains the commercial rights and NIDA retains a license to perform further research. Under a current CRADA, NIDA is working with Teva (formerly IVAX Corporation) to determine

whether talampanel, a compound in clinical testing for treatment of epilepsy, may help cocaine abusers overcome their addiction.

Dr. Vocci says, "Our first 15 years have taught us the importance of developing treatments that patients will accept and readily use, and that medications are most effective in combination with psychotherapy or counseling. We now apply these lessons to all efforts." Looking ahead, Dr. Vocci lists Division goals for the next 5 years:

- Validate the effectiveness of promising medications for cocaine addiction;
- Advance compounds that have shown promise in animal research to clinical testing in people who are addicted to methamphetamine and marijuana;
- Advance a new smoking cessation aid into clinical trials (possibly selegiline, which has shown promise in preliminary studies);
- Determine optimal immunization schedules for nicotine and cocaine vaccines and obtain FDA approval;
- Identify medications to curb cognitive problems that limit patients' ability to benefit from behavioral therapies;
- Continue preliminary clinical studies of interactions between HIV infection, antiviral therapies, and anti-addiction pharmacotherapies and identify interventions that slow the progress of the infection in drug abusers; and
- Collaborate with other branches of NIH and industry partners to test a vaccine for hepatitis C among drug-abusing populations.

"Bringing a new medication to market is a lengthy and expensive endeavor, but physicians and patients need a choice of many treatment options. The progress in anti-addiction pharmacotherapies shows the strength of the dual strategy of medications development, which will continue to provide us with the best hope for novel approaches to treating addiction," says Dr. Vocci. **NN**

Community-Based Treatment Benefits Methamphetamine Abusers

A large California study finds favorable effects for inpatients and outpatients; women's gains are larger.

By Lori Whitten, NIDA NOTES Staff Writer

Methamphetamine abusers can achieve long-term abstinence with the help of standard community-based drug abuse treatment. Nine months after beginning therapy, 87 percent of patients treated for heavy or long-term methamphetamine abuse in California outpatient and residential programs were abstinent from all drugs, according to a NIDA-supported analysis. "In the public dialogue, and even among professionals in the field, one sometimes hears that meth abuse is 'not treatable.' But that view is not borne out by recent clinical trials or our study, which shows that community-based treatment reduces drug abuse and other problems," says lead investigator Dr. Yih-Ing Hser.

Dr. Hser and colleagues at the University of California, Los Angeles analyzed data from the California Treatment Outcome Project (CalTOP), an ongoing study that has followed the progress of adult substance abusers treated at 43 outpatient and residential programs throughout the State since April 2000. The researchers focused on 1,073 patients who reported that methamphetamine abuse was their primary drug problem (572) or that they had abused the stimulant regularly for at least 1 year before beginning treatment (501). Most were in their 30s or younger, White or Latino, unemployed, and on public assistance; most had an arrest history. They had abused methamphetamine for about 9 years, on average, and nearly one-quarter (22 percent) reported injecting drugs at least once. Although 64 percent had children aged 18 or younger, one-third of parents did not live with their children in the month before beginning treatment. One parent in five reported that a child protection court had ordered that his or her children live with someone else, and 6.3 percent

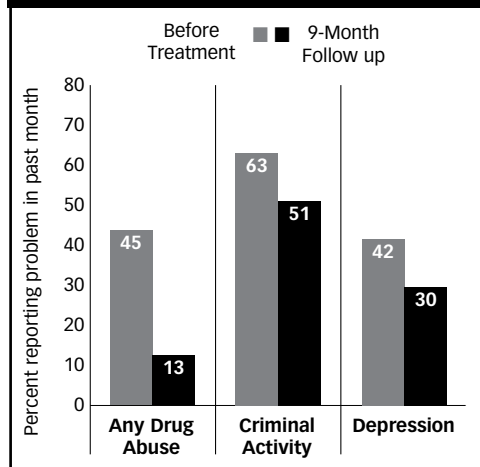
had their parental rights terminated by the State.

The patients received the addiction treatment services routinely provided by each program. These usually included group therapy, with an average of 69 drug-related and 51 alcohol-related sessions during the first 3 months of treatment. On average, the patients also received 22 sessions on dealing with mental health symptoms and 13 addressing psychosocial problems, including family, parenting, and employment.

More than 60 percent of the patients completed 3 months of treatment. Among all the patients in the study—those who finished 3 months and those who did not—the average reported frequency of methamphetamine abuse fell from 2.7 to 0.5 days per month from the start of treatment to 9 months later. The portion who were abstinent from all drugs rose from 55 percent to 87 percent in the same interval, and 68 percent were abstinent and also not incarcerated. Patients improved in all areas—drug and alcohol abuse; mental health symptoms; and employment, family, and legal problems—except one: men's medical problems.

Dr. Thomas Hilton of NIDA's Division of Epidemiology, Services and Prevention Research says these findings should reassure professionals working in the addiction, social services, and criminal justice fields that current therapies work for these troubled patients. "Dr. Hser's findings suggest that treatments available in the community help meth abusers reduce drug abuse and start to get

Abusers Achieve Gains With Treatment



Nine months after methamphetamine abusers began addiction treatment, they had reduced past-month drug abuse and criminal activity, and fewer reported depression.

"Because methamphetamine abusers respond to treatment, getting them into therapy is a top priority. For women, there is added urgency to help them avoid exposing the children they may bear to the consequences of prenatal drug exposure."

their lives back on track, echoing prior research,” he says.

Women’s Experiences

Dr. Hser’s findings confirm gender differences seen in other studies: Women began treatment with more severe psychosocial problems than men (see chart, right) and benefited more. Although treatment retention levels were similar for the two sexes, the women made greater gains in the areas of family relationships and medical problems, while achieving similar improvements in all other areas at the 9-month followup. The women’s better outcomes may have resulted in part from more intensive services (see chart below); as well, Dr. Hser says that many women in the study had a powerful motivator—family. “Many were trying to maintain or regain custody of their children by demonstrating improvement during treatment. Others had ‘hit bottom,’ saw how drug abuse was hurting their families, and decided to make a change,” she says.

“Because methamphetamine abusers respond to treatment, getting them into therapy is a top priority. For women, there is added urgency to help them avoid exposing the children they may bear to the consequences of prenatal drug exposure,” says Dr. Hser.

WOMEN RECEIVE MORE SERVICES IN SOME AREAS

For some problems, women received more services than men during the first 3 months of treatment.

Services	Women (No. of interventions [†])	Men (No. of interventions [†])
Employment*	4.6	2.3
Family [‡]	6.5	4.6
Mental Health [‡]	23.6	19.9
Parenting*	4.2	1.7

[†] Includes counseling sessions, medical appointments, and prescriptions. * Outpatients. [‡] Outpatient and residential.

For some problems, women received more services than men during the first 3 months of treatment.

Dr. Hser and her colleagues continue to analyze CalTOP data, aiming to determine the longer-term impact of therapy and identify ways programs can improve outcomes. “Enhancing psychiatric, parenting, and employment services would better match patients’ needs, and my

Men, Women Experience Different Problems

Family and Social Circumstances	Women, % (n=567)	Men, % (n=506)	Total, % (N=1,073)
Children living with someone else by court order	29.3	9.9	20.1
Parental rights terminated	10.1	2.2	6.3
Family abused substances	21.7	10.5	16.4
Physically abused (past month)	5.5	1.8	3.7
Sexually abused (past month)	2.5	0.6	1.6
Employed	23.8	43.9	33.3
On public assistance	63.1	37.0	50.8
Criminal Justice System Involvement			
On parole	4.4	12.7	8.3
On probation	32.3	37.6	34.8
Ever arrested	76.7	88.3	82.2
Arrest in past year	36.7	45.1	40.6
Criminal activity (past month)	55.2	71.7	63.0
Psychiatric Symptoms (Past Month)			
Serious depression	38.8	29.8	34.6
Difficulties with understanding, concentrating, remembering	36.2	26.5	31.6
Suicidal thoughts	11.3	6.3	9.0
Prescribed psychiatric medicine	21.3	15.4	18.6

Women beginning treatment for methamphetamine abuse reported more psychosocial problems, while men reported more crime and criminal justice involvement.

team plans to study the relationship between help for these problems and longer-term outcomes,” says Dr. Hser. They also plan to investigate whether women-only treatment is more effective for pregnant methamphetamine abusers than mixed-gender programs.

“The field needs more research following meth abusers over time to get a picture of the long-term outcomes of treatment, relapse episodes, and whether these patients require additional support to sustain gains made during therapy,” says Dr. Hilton. “Because the availability of community health and social services varies across States, we cannot generalize the findings from one State, such as California. We need data from across the country,” he adds.

Source

- Hser, Y.-I.; Evans, E.; and Huang, Y.-C. Treatment outcomes among women and men methamphetamine abusers in California. *Journal of Substance Abuse Treatment* 28(1):77-85, 2005. **NN**

Treatment During Work Release Fosters Offenders' Successful Community Reentry

Long-term studies are helping to determine the most effective drug treatment protocols for prisoners in transition.

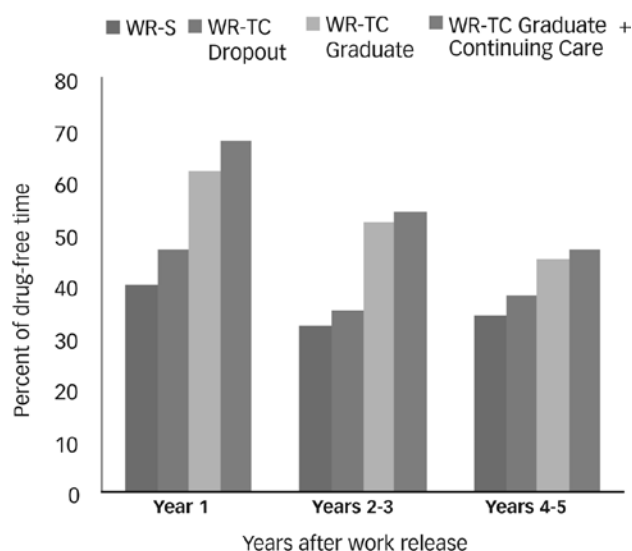
By Lori Whitten, NIDA NOTES Staff Writer

Addiction treatment for prisoners during the pivotal time when they are returning to the community has a strikingly persistent benefit and may create a 'turning point' that helps them stay off drugs and out of trouble, NIDA researchers have concluded after tracking the progress of more than a thousand released offenders. The investigators found that prisoners who participated in drug abuse treatment during a work-release program were three times as likely as untreated peers to remain drug-free up to 5 years. Treatment during work release delayed relapse and resulted in more drug-free time during the followup period. Attendance at continuing weekly group sessions following completion of work-release treatment further enhanced outcomes up to 3 years.

Dr. Clifford Butzin, a co-investigator of the study led by Dr. James Inciardi, at the University of Delaware compared the effectiveness of therapy given in different stages of incarceration, release, and reintegration into the wider community. Their project was part of the State's efforts to offer criminal justice-related treatment programs in three stages—during prison, work release, and parole. In 1990, Delaware established a work-release treatment program to ease the prison-to-community transition with funds from a NIDA treatment demonstration grant. The program utilizes the same therapeutic community model that is the format for Delaware's in-prison treatment. In the mid-1990s, the State added a continuing care component designed to help offenders who have completed work release adapt to living in the community with criminal justice supervision.

The research team analyzed the outcomes of 1,122 drug-involved offenders who participated in work release between 1991 and 1998 and in any followup. The participants' (80 percent male, 72 percent African-American) risk profiles included characteristics typically associated with relapse to drug abuse and crime: extensive criminal histories, low rates of marriage, and substantial unemployment before prison (see chart, next page). The investigators assigned each participant to either standard work-release (WR-S) or the work-release therapeutic community (WR-TC). Because WR-TC slots were limited, priority for them was given to participants who had graduated

Greater Participation In Treatment Increased Drug-Free Time for Most of Followup Period



During the 5 years after prison release, Delaware offenders receiving treatment in a work-release therapeutic community (WR-TC) demonstrated more drug-free time than those in the standard work-release program (WR-S). For the first two followup periods, percentage of drug-free time increased with greater participation in treatment. Beginning 3 years after treatment, the four groups were not significantly different from each other; however, participants in WR-TC demonstrated more drug-free time than those in WR-S.

from the in-prison therapeutic community or whose sentence required treatment as a condition for release.

The participants assigned to the WR-S program served the last 6 months of their sentences working for pay in the community and spent their nonworking hours in a secured residence, but received no formal intervention focused on drugs. Participants in the WR-TC intervention served the last 6 months of their sentences in a secured TC—a "family setting"—in which peers in recovery help participants develop a sense of accountability for their behavior and change negative patterns that lead to drug

abuse. They concentrated on treatment goals, performed assigned duties in the residence, and attended group and individual counseling sessions during the first 3 months of the program. They also participated in mock interviews and seminars on job seeking, started looking for work and housing, opened bank accounts, and developed household budgets. During the subsequent 3 months, they worked in the community and continued therapy during nonworking hours. WR-S participants received no additional services.

Benefits of Work-Release Treatment

After completing work release and returning to the community, WR-TC participants continued treatment for at least 6 months. They attended weekly group sessions at the TC, visited a counselor once a month, and were encouraged to spend at least 1 day a month at the facility.

The investigators interviewed participants at work-release initiation and completion and at 18-, 42-, and 60-month followup points, confirming abstinence reports with urinalysis. The results showed that WR-TC participants who relapsed took twice as long to do so as WR-S participants (28.8 months versus 13.2 months, on average). After leaving prison, WR-TC participants had higher abstinence rates than WR-S participants (32 percent versus 10 percent). Employment rates were also higher with WR-TC (55 percent) than without (45 percent).

To further analyze the relationships between the levels of treatment and outcomes, the investigators subdivided the two groups into four: those in WR-S; those who participated in WR-TC but failed to complete it; those who completed WR-TC but did not participate in aftercare; and treatment graduates with aftercare. At each followup, each increase in level of care was associated with a higher percentage of time spent drug-free, for most of the followup period (see chart, previous page).

Participants in the WR-TC program typically had abused drugs once a day before incarceration, whereas those in WR-S had abused drugs several times a week. Because of their severe drug problems, more WR-TC participants (32 percent) than WR-S participants (5 percent) had received in-prison treatment. However, the researchers determined that treatment during work release was much more effective than in-prison treatment, contributing the bulk of the advantage attained by the WR-TC group. Treatment during work release halved the likelihood of relapsing, whereas other factors—including treatment before or during prison—did not have a significant impact. “Although addiction treatment episodes have a cumulative effect, several studies have shown that the benefits of treatment during prison seem to fade over time compared with therapy during the prison-to-community transition,” says Dr. Butzin.

Among 690 participants who completed all followup interviews, treatment during work release also reduced

arrest rates over the 5-year period. Rearrest was common in all groups, however, with 77 percent of WR-S participants, 58 percent of WR-TC treatment graduates who did not receive aftercare, and 52 percent of those who also received aftercare facing new charges at some point.

Supportive Environment is Key

“It makes sense that a therapeutic community—a stable residence with a drug-free culture and supportive peers—helps people who are looking for a job and a place to live after prison. Continuing care for prisoners with drug problems during the transition back to the community is essential for sustained recovery and other public health benefits, including reduced spread of HIV/AIDS and hepatitis C,” says Dr. Thomas Hilton of NIDA’s Division of Epidemiology, Services and Prevention Research.

Although the prison-to-community transition is critical and may set the pattern for post-release behaviors, research is needed on the best ways to coordinate social and health interventions with criminal justice supervision. Recognizing the importance of science-based knowledge on the effective components of treatment for this population, NIDA established the Criminal Justice–Drug Abuse Treatment Studies (CJ–DATS) research network with Federal partners in justice and public health. CJ–DATS investigators around the United States, including the team in Delaware, are testing interventions and studying approaches for coordinating services for offenders reentering the community.

Source

- Butzin, C.A., et al. Treatment during transition from prison to community and subsequent illicit drug use. *Journal of Substance Abuse Treatment* 28(4):351-358, 2005. **NN**

Work-Release Participant Characteristics	
Characteristic	Percentage
Ever married	29
Unemployed prior to incarceration	58
Treatment prior to incarceration	72
Incarcerated for drug-related crime*	33
Characteristic	Average Number
Arrests prior to incarceration	9
Prior incarcerations	4
* Does not include crimes committed to obtain money for drugs.	

Most participants in the Delaware work-release program demonstrated a long history of criminal activity, chronic drug abuse, and characteristics associated with high rates of relapse and recidivism.

A Brief Encounter With Peer Educator Can Motivate Abstinence

By Lori Whitten, NIDA NOTES Staff Writer

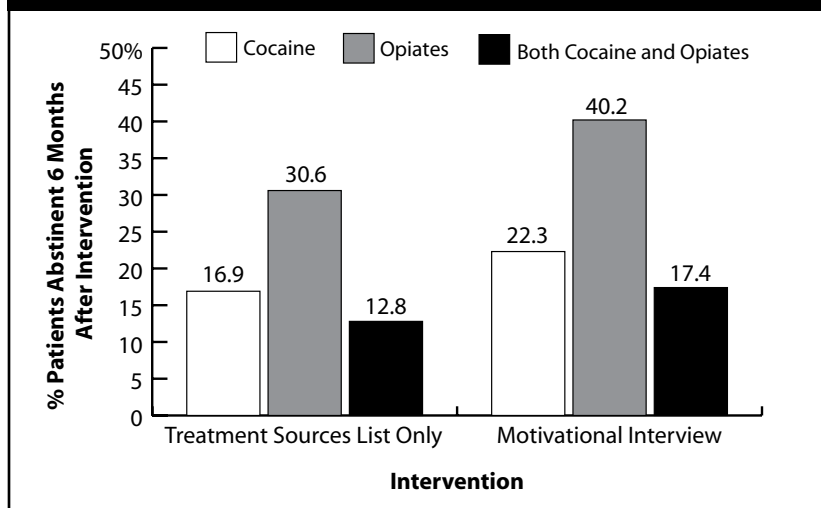
A single meeting with a peer addiction educator during a routine medical visit has helped out-of-treatment cocaine and opiate abusers attain abstinence, report NIDA-funded researchers who conducted a study at three Boston clinics. The peer educators were bilingual individuals in long-term recovery recruited from the same ethnically mixed community as the out-of-treatment drug abusers. The meeting consisted of a structured motivational interview that culminated in a plan for recovery and referrals.

"Talking with a person like yourself—someone who knows your language and culture and views you as an equal, who has successfully recovered from addiction—shows that change is possible and seems to motivate people to get off drugs. It's not a substitute for treatment, but it is a good first step," says Dr. Edward Bernstein of Boston University School of Medicine, one of the lead investigators of the study.

Dr. Bernstein and his coinvestigator Dr. Judith Bernstein hired and trained individuals who had been in recovery for at least 3 years to serve as peer educators and research assistants. This staff then screened 23,669 outpatients who were seeking routine medical care at Boston Medical Center walk-in clinics between May 1998 and November 2000. Altogether 1,175 patients (about 5 percent of those screened) met the criteria for study participation—they reported abusing cocaine, opiates, or both drugs during the past 30 days; scored 3 or higher on the Drug Abuse Severity Test; and were not in addiction treatment or protective custody—and agreed to participate. A research assistant met with each participant to administer further assessments, including an abbreviated Addiction Severity Index (ASI), and an educator then randomly assigned each patient to either an intervention or a control group. Similar proportions of patients in the two groups had abused cocaine (about half), opiates (about 10 percent), or both drugs (33 to 40 percent) during the month before the study (see "Demographic Characteristics of 1,175 Study Participants," on next page).

An educator conducted a motivational interview with each patient in the intervention group. This lasted from 10 to 45 minutes, engaging the patient in a discussion of drug

Motivational Interview During Routine Medical Visit Reduces Drug Abuse



Six months after meeting with a peer addiction educator during a routine medical care visit, patients who participated in a motivational interview had higher rates of abstinence than patients who received a treatment sources list only.

abuse, its consequences, the gap between his or her actual and desired quality of life, and readiness to seek help. The educator concentrated on a few of the patient's problems as identified by the ASI, negotiated a plan for behavioral change, and provided a handout listing treatment resources in the community. The educator was able to convey personal knowledge about the community programs and mention particular people for patients to contact, having visited the organizations as part of his or her training. Ten days after the motivational interview, the educators telephoned patients to review the action plan, ask what happened, and provide additional referrals, if necessary. These calls reached less than a third of patients (31 percent).

Participants assigned to the control group received written advice—"based on your screening responses, you would benefit from help with drug abuse"—along with the handout listing treatment resources. They were not given a motivational interview, and those who expressed interest in the treatment programs were merely encouraged to call a number from the handout. No followup call was attempted with these patients.

Results at Six Months

All participants, both the intervention group and controls, were given appointments to return to the clinic for followup 6 months after their original assessments. The team's research assistants tracked down no-shows by using the clinic's appointment system and visiting shelters and sites frequented by drug abusers. Altogether, they reached 962 (82 percent) of the 1,175 participants. Ultimately, 184 of these patients were excluded from the data analysis, either because hair samples taken at study entry did not confirm their initial reports of drug abuse, or because they did not give samples at followup.

Among the remaining 778 (66 percent of the original sample), 22.3 percent of those who had participated in the motivational interview had been abstinent from cocaine for at least 30 days at the time of the followup interview, compared with 16.9 percent of those who had received just the referral list. The motivational intervention was associated with superior abstinence rates among the subgroups of participants who abused opiates (40.2 percent versus 30.6 percent) and both cocaine and opiates (17.4 percent versus 12.8 percent). These differences occurred even though patients in the motivational interview group had more severe medical and drug-related problems and reported more psychiatric conditions at the beginning of the study.

About 40 percent of patients in each group reported that they had participated in formal treatment with a health care professional during the 6 months between the initial assessment and followup. This similarity in rates of treatment suggests that the brief motivational encounter with the

peer educator was beneficial in itself, and not because it prompted participants to seek therapy. Ninety percent of the patients who said they received professional help underwent detoxification but did not enter ongoing addiction therapy to prevent relapse, a finding the researchers attribute in part to lack of access. "During the study, our patients had very limited access to public methadone treatment, which many had requested," says Dr. Edward Bernstein.

About half the patients in each group who achieved abstinence cited the peer educator as a source of help. The investigators believe patients viewed these individuals as role models for abstinence, which may prompt some to reduce drug abuse even without a motivational interview. "Doctors and patients are not equal, especially when there are language, class, and culture differences. Add drug abuse to the mix, and you usually get 'shaming and should-ing,' which makes patients feel inferior and close down," says Dr. Judith Bernstein. Because of their combination of training and life experiences, peers seemed to inspire optimism about the prospect for recovery, even in patients who felt that others had given up on them. Other sources of support included family, mentioned by 50 percent of patients who achieved abstinence, and self-help groups (68 percent).

Peer Educators Welcomed

Clinic staff at the Boston Medical Center welcomed the study's structured effort to deal with drug abuse, which is a serious problem in the community. They appreciated the fact that the program fit unobtrusively into routine care. "Most doctors don't feel they have the time or training to deal with substance abuse and are happy to suggest that patients see the peer counselor," says Dr. Edward Bernstein. An emergency room physician, Dr. Bernstein plans next to implement and evaluate a peer counseling intervention at five emergency centers.

"It's promising to see reduced drug abuse among these vulnerable patients, many of whom were homeless and unemployed," says Dr. Dorynne Czechowicz of NIDA's Division of Clinical Neuroscience, Development and Behavioral Treatment. Previous studies have demonstrated that alcohol-addicted patients benefit from screening and brief motivational interviews in primary-care settings, but few investigations have involved drug abusers. "More research is needed, but these findings suggest that peer educators can play an important role in busy clinical environments and enhance outreach to abusers of cocaine, opiates, and perhaps other drugs," she says.

Source

- Bernstein, J., et al. Brief motivational intervention at a clinic visit reduces cocaine and heroin use. *Drug and Alcohol Dependence* 77(1):49–59, 2005. **NN**

Demographic Characteristics of 1,175 Study Participants

Characteristic	%
Female	29
Race	
African-American	62
Hispanic	23
White	14
Born in the United States	82
Homeless	46
Reported psychiatric problems	24
Education less than high school	38
Employed	17
Had health insurance coverage	66
Never participated in substance abuse treatment	54

The research team worked with outpatients seeking routine medical care at Boston Medical Center walk-in clinics.

Telephone-Based Continuing Care Sustains Abstinence

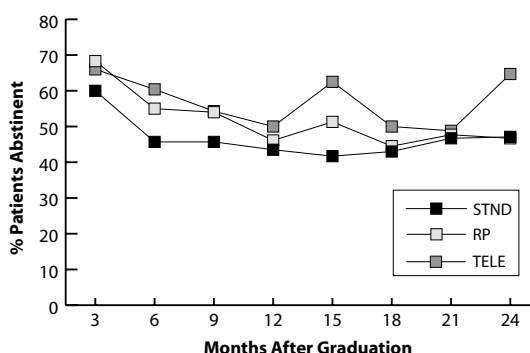
By Lori Whitten, *NIDA NOTES* Staff Writer

Telephone-based continuing care, in which an addiction counselor supports patient recovery with 15-minute calls once a week, can be as good as or better than face-to-face care at helping most patients maintain abstinence after intensive outpatient treatment (IOP). In a recent NIDA-funded study, the benefits of a telephone support protocol were evident nearly 2 years after the last call for all but the 20 percent of patients with severe addiction problems that did not resolve during IOP.

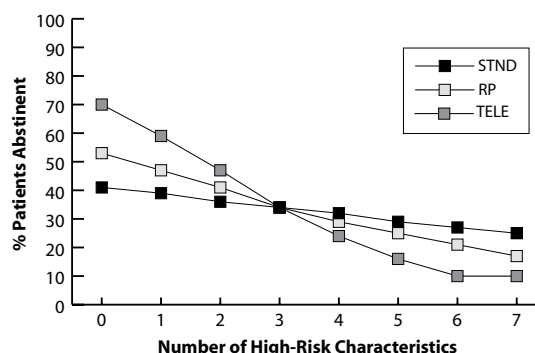
"Telephone-based continuing care does not require transportation or interfere much with work or child-care responsibilities, and this flexibility may help patients stay engaged in recovery and maintain the gains achieved during initial inpatient or outpatient treatment," says Dr. James McKay, lead researcher of the study.

Dr. McKay and colleagues at the University of Pennsylvania, the Treatment Research Institute in Philadelphia, and Brandeis University worked with two Philadelphia-area outpatient addiction programs. Patients seeking treatment in these programs received about 9 hours of outpatient group therapy each week for 1 month, on average. The therapy concentrated on overcoming denial of substance abuse, learning about the addiction process and cues to relapse, and beginning self-help participation. Dr. McKay and colleagues recruited patients who "graduated" from therapy—that is, continued in the IOP and achieved abstinence in the

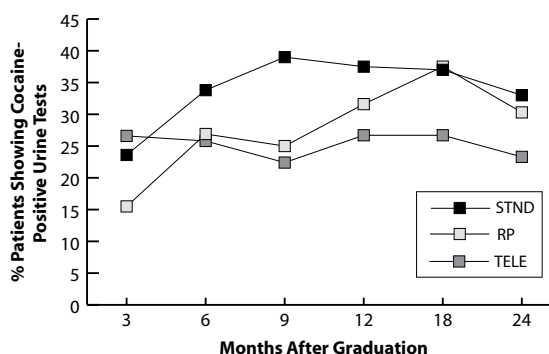
Telephone Counseling Helps Outpatient Treatment Graduates Stay Abstinent



Two years after graduating from intensive outpatient treatment, more patients who participated in telephone-based continuing care (TELE) had maintained abstinence during the previous 3 months than those receiving standard group counseling (STND). The percentage of abstinent patients did not differ between TELE and relapse prevention (RP) continuing care.



Throughout the study, patients with four or more characteristics reflecting severe addiction were better able to maintain abstinence if they participated in STND compared with TELE.



The percentage of cocaine-positive urine samples did not increase as quickly during the follow-up for TELE patients as it did for those who participated in RP, with a similar trend for TELE compared with STND.

All patients participated in 12 weeks of continuing care after completing a month of intensive outpatient treatment, and reported outcomes every 3 months during the 2-year followup.

last week—to receive 12 weeks of continuing care and followup for 2 years.

The patients, 359 men and women aged 18 to 65, were typical, in terms of demographics and problem severity, of individuals seeking treatment at publicly funded outpatient addiction programs. Half met the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) criteria for co-occurring cocaine and alcohol dependence, 87 were dependent on cocaine only, and 91 were alcoholic. Thirty percent had met the criteria for a diagnosis of major depression at some time in their lives. When they began treatment, they reported 8 years of cocaine and 18 years of alcohol abuse, on average, and multiple attempts to quit.

Regular Contact With a Therapist Is Crucial

The investigators randomly assigned each patient to one of three continuing care therapies: a face-to-face therapy, either standard group (STND) or relapse prevention (RP); or telephone-based (TELE) counseling. In STND care, the most common approach to continuing care for addiction, 122 patients attended twice-weekly counseling sessions that emphasized overcoming denial and engaging in mutual- and self-help activities. In RP therapy, 135 patients attended an individual session of cognitive-behavioral therapy and then group sessions once a week. In this approach, patients identify situations that prompt substance abuse and work to improve coping responses using structured activities and homework exercises.

In TELE care, 102 patients met with counselors in person the week before beginning the telephone phase to discuss the therapy and receive a workbook with exercises that structured subsequent calls. At a scheduled time each week, they telephoned counselors and talked for 15 to 20 minutes about progress during the previous week, any episodes of substance abuse, participation in self-help and other pro-recovery activities, plans for achieving the next week's goals, and any concerns. Counselors contacted patients who did not call and discussed in a supportive way their reasons for not doing so. To ease the transition from outpatient to continuing care, therapists offered the TELE patients group counseling once a week for a month. Patients struggling with relapse at that point could continue with group sessions; more than a third (35 percent) exercised this option.

The researchers followed up with patients every 3 months throughout the study and contacted 86 percent 2 years after graduation from IOP. At this point, about two-thirds of TELE patients reported abstinence during the previous 3 months, compared with about half of those who had participated in STND. An analysis of urine samples from

the cocaine-addicted patients showed an overall increase in the percentage of cocaine-positive samples during the followup period, but the increase was more rapid among RP participants than TELE participants. The TELE group had higher abstinence rates than STND throughout followup. Patients who participated in TELE maintained the gains of IOP even though they received about half as much therapeutic contact (428 minutes) as those receiving STND or RP (845 and 861 minutes, respectively).

“Continuing care benefits people in recovery in several ways, but regular contact with a therapist is crucial for patients with a chronic condition, and especially helps patients who have relapsed get back into treatment,” says Dr. Dorynne Czechowicz of NIDA’s Division of Clinical Neuroscience, Development, and Behavioral Treatment. Although larger studies with more diverse patients are needed, Dr. McKay and his colleagues laid important groundwork, she says.

Face-to-Face Care for Severe Problems

Some patients need more contact with a counselor than telephone-based continuing care affords to maintain recovery. To identify these patients, Dr. McKay and his colleagues examined the link between outcomes and seven patient characteristics: co-occurring addiction to alcohol and cocaine at the beginning of IOP; any alcohol use, any abuse of cocaine, minimal attendance at self-help meetings, below-average social support during IOP; and a lack of commitment to complete abstinence, and low self-efficacy for recovery at the end of IOP.

Patients who demonstrated three or fewer of the characteristics—about 80 percent of the study population—did at least as well with TELE continuing care as with the other two approaches. But the remaining patients, those who met the criteria for co-occurring addiction at the beginning of treatment and did not achieve the main goals of IOP—abstinence from cocaine and alcohol during treatment, commitment to abstinence, and participation in self-help programs—were at high risk for relapse and showed better outcomes with STND continuing care, relative to TELE, during most of the followup. The findings suggest that TELE may be inappropriate for patients with more severe addiction problems until they demonstrate stable abstinence from drugs and alcohol, says Dr. McKay.

Flexible Continuing Care

“Some practitioners are developing flexible arrangements to engage and retain more patients in continuing care,” says Dr. McKay. Flexibility in the practical sense—the ability to call one’s counselor from any location—extends participation in continuing care, not only to busy people,

but also to those living in rural areas or who have lost driver's licenses.

Telephone-based care is one way that a treatment intervention can respond to each patient's progress during recovery; it gives counselors the flexibility to intensify care if the patient is struggling to maintain abstinence. "Clinicians managing other chronic disorders—for example, hypertension and cancer—are using progress during initial treatment to determine subsequent care. It's not a new therapeutic approach, but it is novel to addiction treatment," Dr. McKay says.

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Successful Drug Abuse Treatment in Adolescents Should Address Co-Occurring Mental Health Problems

By Lori Whitten, *NIDA NOTES* Staff Writer

Adolescent substance abuse patients with co-occurring emotional and behavioral problems are more likely than peers without coexisting psychiatric conditions to relapse in the year following treatment, a NIDA-funded study has found. “We must improve identification of co-occurring psychiatric disorders among substance-abusing teens and move away from a ‘one size fits all’ approach to therapy, or treatment gains will remain limited for these vulnerable youth and their families,” says Dr. Cynthia Rowe at the University of Miami School of Medicine in Florida, who led the study.

Following 182 adolescents for a year after substance abuse treatment, Dr. Rowe and her colleagues found that those with co-occurring externalizing disorders—a combination of aggressive and delinquent behaviors including persistent lying, stealing, fighting, and destroying property—recovered more slowly than those without psychiatric disorders. Youths with externalizing and internalizing disorders—acting out mixed with anxiety and depression—obtained the least favorable treatment outcomes. Dr. Rowe says this combination of symptoms often relates to multiple problems in life and indicates psychiatric severity—the best predictor of substance abuse treatment outcomes in adults. “Our results mirror those seen in adults: People with more severe psychiatric problems show a significantly diminished response to substance abuse treatments of known effectiveness,” says Dr. Rowe.

All the youths had been referred to substance abuse treatment, almost 85 percent by the juvenile justice or child service systems; they ranged in age from 12 to 17 at the beginning of the study. Participants received manualized treatment—cognitive behavioral therapy (CBT) or multidimensional family therapy (MDFT)—in weekly office-based sessions for an average of 10 weeks. At the outset of the study, the participants’ reports of substance abuse frequency in the past month averaged 12.7 days; by the end of the treatment, this figure dropped by 2.5 days. Six months after treatment, past-month substance abuse had fallen another 2.5 days; at the 12-month followup, abuse incidence had dropped an additional 2.5 days. The rates and patterns of change, however, varied depending on coexisting psychiatric disorders.

Substance abusers with no co-occurring disorders (12 percent of the study population) showed the best long-term outcomes. Although initially unresponsive to treatment,

they markedly and rapidly reduced substance abuse between the 6- and 12-month followups—changing at a rate approximately 1.5 times that of peers with co-occurring externalizing disorders (35 percent of the study population), who also were initially unresponsive to treatment and also recovered. Youth demonstrating mixed externalizing and internalizing symptoms

(48 percent of the study population) showed the opposite pattern. Initially improving in response to therapy, they had relapsed to pretreatment levels of substance abuse a year later. The responses did not differ in patients participating in CBT and MDFT.

Dr. Melissa Racioppo of NIDA’s Division of Clinical Neurosciences, Development and Behavioral Treatments says CBT and MDFT are very effective treatments for most adolescent substance abusers (see “Family-Based Treatment Programs Can Reduce Adolescent Drug Abuse,” *NIDA NOTES* Vol. 17, No. 4, p. 7). Poorer treatment outcomes among people with co-occurring psychiatric disorders suggest that therapists may need to tailor substance abuse treatment for the patient’s particular psychiatric condition, although the necessary level of specificity is not clear. “To adapt treatments for people with co-occurring psychiatric disorders, researchers must link particular therapeutic processes with outcomes,” she adds—something Dr. Rowe and her colleagues plan to do in future studies.

“Looking within the therapeutic process may help us discover what must happen to realize recovery from substance abuse. Effective components of therapy may vary for adolescents with different co-occurring mental health problems, and identifying such mechanisms of change may help us develop better interventions,” says Dr. Rowe.



Girls Had More Severe Problems

Most (82 percent) of the study's participants were boys; however, girls were overrepresented in the group with the least favorable treatment outcomes. More girls (83 percent) than boys (44 percent) displayed externalizing and internalizing disorders. Dr. Rowe says the pattern is familiar to clinicians across the country—there are typically more girls among the substance abuse patients with pronounced problems and disorders. “By the time a girl with substance abuse problems is referred to treatment, she is usually in considerable distress and experiencing severe psychiatric symptoms and relationship problems. Family, school, and legal problems will continue unabated without better identification, referral, and treatment of these vulnerable girls,” says Dr. Rowe. Dr. Racioppo emphasizes the need for more research on differences in how boys and girls develop and manifest behavior problems. Troubled youth often have experienced family conflict and instability in relationships, but boys and girls may react differently. Studies indicate that females tend to turn their stress inward, developing anxiety and depression, which are often unnoticed by adults. Dr. Racioppo says girls tend to act out in ways that don't necessarily grab the attention of adults—through sexual behavior, for example—whereas boys externalize in ways that are more obvious, such as fighting. “To improve identification and treatment outcomes of adolescents with co-occurring psychiatric disorders, we need to study gender differences in the root causes and expression of behavioral and emotional problems,” she says.

Source:

- Rowe, C.L.; Liddle, H.L.; Greenbaum, P.E.; and Henderson, C.E. Impact of psychiatric comorbidity on treatment of adolescent drug abusers. *Journal of Substance Abuse Treatment* 26(2):129-140, 2003. **NN**

Depression Elevates Suicide Risk in Substance-Abusing Adolescents

A recent NIDA-funded study highlights the need for substance abuse counselors to be aware of depression and suicide risk in their adolescent patients. Drs. Thomas Kelly, Duncan Clark, and colleagues at the University of Pittsburgh School of Medicine identified 85 suicide attempters in a series of 503 substance-abusing teenagers studied from 1991 to 2000. Most of the teenagers abused alcohol (88 percent) and marijuana (80 percent). A large majority—87 percent—of those who had attempted suicide were diagnosed with major depression using the *Diagnostic and Statistical Manual, 4th Edition* (DSM-IV) criteria. Among substance-abusing teens who did not attempt suicide, major depression was diagnosed in only 40 percent. Girls were three times more likely to have attempted suicide than boys. Among the attempters, one-third of girls and one-tenth of boys reported multiple attempts—a finding consistent with general patterns of suicidal behaviors.

“Clinicians who work with adolescent substance abusers may not automatically think about suicidal behavior as something to watch for in their clients, but it's definitely a concern—especially for youth with co-occurring psychiatric disorders,” says Dr. Lynda Erinoff of NIDA's Division of Epidemiology, Services and Prevention Research. There is an association between substance abuse, co-occurring psychiatric disorders, and suicidal behavior in adults and adolescents, but Dr. Erinoff explains that it's difficult to establish causal factors and sequencing of these problems.

Dr. Clark and his colleagues are pursuing another avenue of research that may provide clinicians with a biological marker to help assess patients' risk of suicidal behavior. In a recent prospective study, Dr. Clark found that depression and low blood levels of tryptophan—an amino acid found in protein-rich foods such as turkey and milk—were associated with increased suicide risk in adolescents who abused alcohol. Other studies have suggested that depleted tryptophan is related to depression and impulsivity, which seem to increase the risk for suicidal behavior. If additional studies corroborate the predictive value of this potential biological marker, clinicians could have a blood test to augment their behavioral assessment that a patient may be at risk for attempting suicide.

Sources:

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Economists Offer Program for Costing Out Drug Abuse Treatment

By Marion Torchia, NIDA NOTES Contributing Writer

NIDA-supported economists are offering drug treatment program administrators a comprehensive program to estimate their costs. The Drug Abuse Treatment Cost Analysis Program (DATCAP) features materials and a method to capture and put dollar values on the full range of treatment resources. Along with analyzing their own economic operations, administrators eventually will be able to use a nationwide DATCAP database to compare their costs with those of similar programs, become more efficient, and achieve better treatment outcomes. Dr. Michael T. French of the University of Miami in Coral Gables, Florida, one of the system's designers, says that ultimately, the database should provide answers to the questions asked by cost-conscious public agencies and insurers: How much do today's drug treatment programs cost? What are the most cost-effective treatment approaches? Which programs return the greatest net benefits?

DATCAP Features

Administrators can download DATCAP survey forms and user manuals free of charge from www.DATCAP.com. DATCAP's developers note, however, that most programs will require the services of an economist trained in cost analysis and program evaluation to obtain the most useful results.

DATCAP captures both accounting costs (the costs usually entered on an institution's financial statements, such as outlays for labor and supplies) and economic costs (all the resources a treatment center uses to serve its patients). Economic costs include resources that are partially subsidized or made available at no charge, such as volunteer labor.

Mean Patient Flow and Costs of Substance Abuse Treatment Programs

Outpatient Programs

Information gathered between 1993 and 2002 from 53 outpatient programs.

Program Type (Number Surveyed)	Average Length of Stay, weeks (SD)	Average Daily Census (SD)	Total Annual Economic Cost (SD)	Weekly Economic Cost Per Client ¹ (SD)	Economic Cost Per Treatment Episode ² (SD)
Methadone clinics (11)	99 (53)	388 (186)	\$1,684,254 (\$674,444)	\$91 (\$33)	\$7,358 (\$3,849)
Standard outpatient (14)	17 (9)	212 (188)	\$1,080,690 (\$757,227)	\$121 (\$85)	\$1,944 (\$1,960)
Intensive outpatient (6)	7 (8)	13 (9)	\$328,007 (\$411,364)	\$462 (\$243)	\$4,445 (\$6,302)
Adolescent outpatient (13)	13 (6)	8 (2)	\$48,170 (\$50,518)	\$194 (\$91)	\$2,678 (\$2,787)
Drug court (9)	46 (20)	205 (184)	\$539,660 (\$136,713)	\$82 (\$43)	\$3,463 (\$2,187)

Residential Programs

Information gathered during the same period from 32 residential programs.

Program Type (Number Surveyed)	Average Length of Stay, weeks (SD)	Average Daily Census (SD)	Total Annual Economic Cost (SD)	Weekly Economic Cost Per Client ¹ (SD)	Economic Cost Per Treatment Episode ² (SD)
Adult residential (18)	13 (14)	34 (21)	\$1,104,189 (\$643,053)	\$700 (\$343)	\$9,426 (\$11,023)
Adolescent residential (1)	8	22	\$1,307,064	\$1,138	\$9,347
Therapeutic community (5)	33 (22)	152 (265)	\$3,330,137 (\$4,821,587)	\$587 (\$194)	\$18,802 (\$12,409)
In-prison therapeutic community (8)	28 (12)	265 (288)	\$1,083,017 (\$1,587,030)	\$55 (\$11)	\$1,534 (\$947)

Source: Roebuck, M.C.; French, M.T.; and McLellan, A.T. (2003).

Notes: All amounts, including dollar amounts, are means. All costs are reported in 2001 dollars.

¹ Total annual economic cost divided by the average daily census, divided by 52.14 weeks.

² Weekly economic cost per client multiplied by the average length of stay.

DATCAP's inclusive cost perspective permits comparison of treatment programs that have very different financial structures.

The program is adaptable to any treatment setting. By focusing on the cost of specific treatment methods rather than on entire programs, it can capture costs in settings that also offer other services. The same questionnaire is provided for inpatient and outpatient services.

“Program DATCAP” gathers detailed information about a program’s resources, revenues, and expenses, and about its clients and the services they receive. “Brief DATCAP” is a less labor-intensive alternative to the full instrument. “Client DATCAP” surveys clients directly and assigns a dollar value to costs they incur as a result of getting treatment, such as travel and child care. Although the DATCAP project is still in its early stages, administrators who use it can identify costs they were unaware of and find opportunities to strengthen their operations.

The Nationwide Database

Dr. French hopes that as program administrators around the country begin to use DATCAP to track their own costs, they will see the advantage of reporting their findings to a central repository. “Only when everyone’s costs are pooled will it be possible for a program to compare itself with other programs,” he says.

To encourage wider participation in the ongoing research on DATCAP, its creators have published some early survey results. Among these, they found that among 85 programs surveyed between 1993 and 2002, methadone maintenance programs had lower labor costs (55 percent of total costs compared with 68 percent for standard outpatient programs) and relatively higher costs for supplies and materials. Not surprisingly, standard outpatient programs were much less expensive than intensive programs: The 14 standard programs reported a mean weekly economic cost per client of \$121; for the intensive programs, the weekly cost was nearly four times that amount—or \$462 per client. However, the intensive programs generally offered a shorter course of treatment, so their mean total cost for a client’s treatment episode was only slightly more than twice the cost of the standard outpatient programs (\$4,445 versus \$1,944).

The new database has limitations, the authors caution. The programs were not selected randomly and are not geographically representative. Also, the costs of a small number of atypical programs sometimes skewed the results. Nevertheless, says Dr. French, the results of the 85 surveys constitute a rich new source of information. “The database will get better as new programs are added, and eventually the cost estimates will be updated continually on the DATCAP Web site,” he says.

Next Step: Link Cost to Outcome

Although program managers find it useful to compare their costs with those of their peers, policymakers are much more interested in the relationship between costs

and the intended program outcomes. Cost-effectiveness analysis and cost-benefit analysis of drug abuse treatment have demonstrated encouraging results. One California study found that \$1 invested in substance abuse treatment saves taxpayers \$7 in future costs, including those related to crime and care for medical problems resulting from drug use. “Evaluating Recovery Services: The California Drug and Alcohol Treatment Assessment (CALDATA),” California Department of Alcohol and Drug Programs, April 1994.

In a recent study using DATCAP, Dr. Jody Sindelar and her colleagues at Yale University in New Haven, Connecticut, found that Philadelphia treatment programs that offered “enhanced care” produced better outcomes with regard to drug abuse compared with those that offered only standard care. However, standard care programs had better results with respect to other treatment outcomes.

Says Dr. Sindelar, “Looking at treatment programs with too narrow a focus may produce misleading results. Reduced drug use is certainly the most direct outcome of treatment, but it is not necessarily the only one, or even the most important one to society. We need to find ways to give appropriate weight to all the outcomes we believe are important. But we believe that combining DATCAP and ASI [Addiction Severity Index] is a good first step.”

Techniques of Economic Analysis of Drug Treatment

- **Cost-Effectiveness Analysis:** A technique for evaluation of clinical outcomes. It asks whether one treatment produces a better outcome at the same cost as another, comparable outcomes at less cost, or if an enhanced outcome is “worth” the additional cost.
- **Cost-Benefit Analysis:** Decisionmakers use cost-benefit analyses in determining how to allocate their budgets. The “cost” part of the analysis estimates the dollars necessary to achieve each alternative policy goal—for example, reducing drug abuse by 10 percent or raising school test scores by 10 percent. The “benefit” part estimates the dollar value of all the positive effects of success—for example, reduced medical costs because of fewer health problems associated with drug abuse, or a better educated, more skillful workforce attracting new industry to the area. All other concerns being equal, the goal that produces the most benefits for the lowest cost gets budget priority.

Dr. William S. Cartwright, an economist with NIDA's Division of Epidemiology, Services and Prevention Research, believes DATCAP is the beginning of something important. "We know more about where the hidden costs are, and we are able to link costs to outcomes. I hope this information will enable us to make better use of scarce resources, toward our shared goal of reducing drug abuse and the problems it causes."

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Adults With Co-Occurring Depression and Substance Abuse Benefit From Treatment of Depression

New evidence is overturning the long-held view that patients with co-occurring mental health and substance use disorders must achieve abstinence from drugs before treatment for depression can begin. There were sound reasons for adhering to this view, including clinician concern about drug interactions and recognition that depressive symptoms brought on by substance abuse are difficult to separate from clinical depression itself. As the field continues to refine screening tools that distinguish the disorders, however, new treatment approaches are being developed and assessed.

In a study that reinforces the need to revisit traditional management of these conditions, NIDA-funded researchers Drs. Edward Nunes and Frances Levin of Columbia University in New York City reviewed 33 years of published literature on the treatment of depression in the context of ongoing substance abuse. They found that antidepressant treatment is not sufficient for these patients, and they emphasize the need to integrate the treatment of depression and substance abuse. The investigators examined 44 placebo-controlled clinical trials published from 1970 to December 2003; 14 followed a rigorous methodology and were included in the study. Drs. Nunes and Levin used meta-analysis—a technique that synthesizes data from similar studies and determines how much particular factors affect outcomes—to examine the effects of antidepressant medication in approximately 850 patients with co-occurring substance abuse. They found that treating the depression of patients with co-occurring substance abuse conveys moderate benefit. Patients who responded to the antidepressant treatment also showed

a reduction in substance abuse. However, cessation rates were generally low, even among studies demonstrating positive effects of antidepressants. Drs. Nunes and Levin suggest that clinicians first treat the depression with an evidence-based psychosocial intervention, followed by antidepressant medication if the depression does not improve.

“The study provides quantitative evidence on the benefit of treating depression in those with co-occurring substance abuse and supports integrated treatment of both disorders. Cognitive behavioral therapy is a good first approach for treating these patients, but the findings show the efficacy of antidepressant medications for patients with coexisting depression and substance abuse,” says Dr. Ivan Montoya of NIDA’s Division of Pharmacotherapies and Medical Consequences of Drug Abuse. Some clinicians worry that treating a patient’s depression distracts attention from treating their co-occurring substance abuse. But Dr. Montoya says, “Patients may attach less stigma to seeking treatment for depression than substance abuse. Clinicians are increasingly finding that they have an opportunity to treat substance abuse in patients who present with depression; now, they have quantitative evidence to support the decision of concurrent treatment.”

Source

- Nunes, E.V., and Levin, F.R. Treatment of depression in patients with alcohol or other drug dependence: A meta-analysis. *JAMA* 291(15):1887-1896, 2004. **NN**

CTN Update: Teamwork Develops Treatment Concept Into Study Protocol

By Barbara Shine, *NIDA NOTES* Contributing Writer

In NIDA's Clinical Trials Network (CTN), researchers and practitioners collaborate in the design as well as the execution of drug abuse treatment studies. Continuous collaboration with treatment providers, a distinguishing feature of the network, ensures a research focus on practical questions that arise in typical patient populations and community treatment settings.

A new study begins when a researcher or treatment provider identifies a clinical need and formulates a solution or intervention to meet it. Research ideas are accepted only if they coincide with public health priorities and meet two standards—feasibility and sustainability. A feasible research concept is one that can be tested in established, community-based treatment programs with varied patient populations. To meet the sustainability standard, the proposed intervention should be possible to continue in community treatment programs equipped with a realistic complement of resources after study completion. The concept proposal also must stand on a foundation of previous supporting research. Once it meets these criteria and gains approval within CTN and by NIDA, the proposal is ready to move on to protocol development and final NIDA approval and funding.

An example of the pragmatic approach to research design is the recently completed CTN-sponsored study "Motivational Incentives for Enhanced Drug Abuse Recovery." This work is based on the general idea that rewards—including supportive words, praise, money, or desirable objects—for a particular behavior promote like behavior in the future. Two protocols emerged: one for implementation in methadone maintenance clinics and another for study in clinics using treatments other than methadone maintenance.

"There were two key points to negotiate in designing these trials," says Dr. Maxine Stitzer of Johns Hopkins University School of Medicine in Baltimore, the principal investigator for both motivational incentive protocols. "The first was selection of the drug target. Previous incentive studies had targeted only one drug, but we targeted both cocaine and methamphetamine to address regional differences in stimulant abuse. We added alcohol as a primary target and opiates and marijuana as secondary drug targets to emphasize the importance of giving up all drugs, not just the particular one that brought the patients into



Clinical Trials Network

treatment. Patients could draw chances to win prizes when their breath and urine samples were negative for target drugs."

"The second big issue was how much the prizes should be worth," says Dr. Stitzer. "Early studies in research centers cost upwards of a thousand dollars per patient for prizes; community treatment providers made it clear they needed an

effective motivational approach that would not exhaust their much smaller budgets. People in our study drew chances to win a range of prizes—from bus tokens, to \$20 grocery vouchers, to compact disc players—that were more realistic for community treatment centers."

Members of the protocol development group benefited from meeting with Dr. Nancy Petry, an investigator who conducted similar studies at the University of Connecticut in Farmington, and with several of her clinical staff and patients. "We really gained valuable insights and heard firsthand how the patients' motivations changed over the course of their treatment, from working for prizes to working for their own good," says Dr. Stitzer.

Once NIDA approved the motivational incentives protocol, investigators implemented the study in 14 treatment programs with a total of about 800 patients. Preliminary analysis of the data suggests that the addition of reward systems to standard therapy will improve outcomes for drug abuse patients. Once Dr. Stitzer and her team analyze and publish the results, clinicians will know whether motivational incentives are truly an effective adjunct to current therapies.

For More Information

To learn more about CTN protocols, including studies that are now recruiting patients, visit the NIDA Clinical Trials Network Web site, www.drugabuse.gov/CTN. Both English and Spanish brochures for patients and physicians are available for download, and the site lists contact information for all regional research and training centers and clinical trials.

Dr. Petry's research is highlighted in "Fishbowls and Candybars: Using Low-Cost Incentives To Increase Treatment Retention" (*NIDA Science & Practice Perspectives*, Vol. 2, No. 1, p. 55), which is also available on NIDA's Web site, www.drugabuse.gov. **NN**

Testing New Treatments in the Nation's Clinics

In NIDA's first 30 years, its research programs produced many promising new medications and behavioral treatments. Yet, as in other areas of medicine, new and improved treatments for drug abuse have often



taken too long to make their way into wide clinical use. In 1999, NIDA acted to bridge the critical gap between research and practice by launching the largest initiative in its history—the National Drug Abuse Treatment Clinical Trials Network (CTN).

The CTN embraces an ambitious plan to accelerate the transfer of new science-based behavioral and pharmacological approaches into treatment: to create a national research-practice infrastructure to test and modify promising treatments in community treatment programs, rather than specialized research settings, and rapidly transfer those proven effective into clinical practice. The network also seeks to develop new treatments that reflect the practical knowledge of the clinic, thus accelerating their acceptance and application in practice.

Beginning with 5 regional research and training centers, each linked to as many as 10 community treatment programs, the CTN brought researchers into community clinics to work alongside practitioners in testing research-based treatments. In little more than a year, NIDA and the pioneering group of university researchers, treatment programs, and practitioners built the organizational and procedural foundation for the CTN, selected promising pharmacological and behavioral approaches, developed standardized clinical protocols, and began testing them in trials with a variety of patients at multiple sites.

The CTN now encompasses 17 regional research and training centers and 115 community treatment programs across the Nation. Minorities, pregnant women, adolescents, and drug abuse patients suffering from post-traumatic stress disorder or depression are among the pool of nearly 9,000

drug abuse treatment patients in 27 States who have or will soon participate in 22 clinical protocols—some under way, some still being refined—for a variety of new treatment approaches. Medication trials range from assessing the effectiveness of buprenorphine in detoxifying opiate-dependent patients to determining whether a combination buprenorphine/naloxone tablet can help treat heroin-addicted adolescents. Behavioral treatment trials take many approaches: tests using motivational enhancement techniques or tangible incentives for staying drug-free to enhance standard counseling approaches, several HIV risk-reduction interventions, and an intervention to help patients in drug abuse treatment stop smoking.

Taking Prevention Programs Into Our Communities

Although a relatively new science, drug abuse prevention has already yielded a bounty of programs capable of steering many young people away from drug use. As with drug abuse treatments, however, many of these research-proven programs stayed on the shelf, while simpler, less effective approaches were used. Even when such approaches were selected, they often were not delivered to maximum effect.

Taking a cue from the CTN, NIDA began to partner prevention researchers and practitioners to establish research-based programs in the Nation's communities. A major component of NIDA's recently launched broad-based National Prevention Research Initiative instituted four



Community-based prevention programs teach children strategies to avoid drug initiation and other harmful behaviors.

large-scale field trials of proven drug abuse prevention approaches. These trials find scientists and practitioners collaborating to deliver a research-tested intervention to diverse groups of children and adolescents in urban, suburban, and rural sites. Each trial examines factors with potential impact on a program's effectiveness, such as how different training methods affect its delivery or how accurately community service programs deliver an intervention to different groups in various settings.

Results of these joint research-practice studies will reveal practical barriers to widespread dissemination and implementation of research-tested programs. Equally important, they will point to how programs can be adapted to meet the needs of local communities while still reducing drug use. Ultimately, blending science-based knowledge with community realities will produce more practical prevention programs that will be used by more communities to divert children and adolescents from initiating drug use.

Advancing the Frontiers of Addiction Research and Practice

The first three decades of NIDA leadership ushered drug abuse science toward full maturity. The result: profound and practical insights into the complex biological, behavioral, cognitive, and environmental interactions that influence every aspect of drug abuse and addiction. Practitioners now have many effective tools for preventing and treating drug abuse and addiction and their costly public health and social consequences. Yet, much work remains. Too many children and adolescents continue to experiment with drugs, putting themselves at risk for addiction. Research to speed the development and application of prevention strategies stands at the forefront of NIDA's priorities.

Additional NIDA research initiatives continue to address the critical need for treatments for drug abusers who suffer from mental illnesses or abuse multiple substances, including nicotine and alcohol. And more broadly effective prevention and treatment approaches will enable NIDA to fulfill its public health mission of reducing the severe health consequences of addiction, including increased risk of contracting and transmitting infectious diseases.

NIDA is applying revolutionary new techniques in molecular biology, brain imaging, and cognitive neurosci-

ence to these outstanding issues in drug abuse etiology, prevention, and treatment. For example, neuroscientists in the Institute's proteomics program are using 3-dimensional imaging technology to map how distinct proteins in different regions of the human brain function, interact, and change from initial drug use through the transition to addiction. Such research promises new understanding of the molecular mechanisms of drug addiction and the underlying processes of normal and diseased brain function. While offering important new targets for the next generation of therapeutic approaches, this research may someday allow clinicians to match an intervention to a patient's physiological or genetic traits.

The role that interactions between genetic factors and the environment play in vulnerability to addiction is another area of promise recently opened up through advances in scientific technologies. For while genes and the proteins they produce may increase or reduce the risk of addiction, they do not function in isolation. Using brain-imaging techniques, researchers recently found that social environment can modify monkeys' neurobiology, thereby reducing their likelihood of self-administering drugs.

In the study, housing conditions and social interactions altered the genetic expression of proteins in the brain that enable animals, including humans, to experience pleasure and the effects of drugs.

The complexity of drug abuse questions that have come to the fore requires investigation from multiple perspectives. To achieve this goal, NIDA has launched broad research initiatives involving Federal, State, and local government agencies; scientists from

many different fields; public and private health service providers; prevention and treatment professionals; and private pharmaceutical companies. One key feature of these collaborations is their emphasis on the resources and practical needs of communities at all research stages—from basic discovery through intervention development to actual trial and integration in community prevention and research programs. Examples of collaborative initiatives include the following.



Environmental factors, such as a positive home life, may boost brain chemicals that offer resistance to drugs' reinforcing effects.

Transdisciplinary Research Centers. Teams of researchers pool their expertise to search for new knowledge about the interplay of individual, cognitive, social, and environmental circumstances in fostering drug abuse and its many harmful consequences. NIDA currently supports transdisciplinary centers in prevention and tobacco use research.

In the tobacco use centers, NIDA, with the National Cancer Institute and the Robert Wood Johnson Foundation, supports investigation of all aspects of tobacco use, from factors that influence initiation through those that aid cessation. The goal is to discover new ways to prevent and treat nicotine addiction, particularly in adolescents.

Collaborating to Combat Tobacco Use and Nicotine Addiction

In July 1998, NIDA, with the National Cancer Institute (NCI), the Centers for Disease Control and Prevention, and The Robert Wood Johnson Foundation (RWJF), sponsored "Addicted to Nicotine," a national research conference on tobacco use and nicotine addiction. This event shed new light on the complexity of research challenges posed by nicotine addiction. Informal conversations among researchers and policymakers highlighted the need for an innovative research approach to meet these challenges. Within a year, this dialogue yielded a proposal: develop Transdisciplinary Tobacco Use Research Centers (TTURCs) to foster collaborations among scientists across many disciplines and allow them to investigate tobacco use and nicotine's effects at levels ranging from molecular genetics to peer interactions. By October 1999, NIDA and NCI announced the first TTURC awards and committed about \$70 million to the effort over 5 years. RWJF committed an additional \$14 million.

Today, investigators at seven TTURCs across the country are carrying out the research agenda that gave birth to the centers. Their collaborations have produced scores of published studies that advance our understanding of nicotine's addictive effects and the scope of influence smoking has on the Nation's health. Consider the following research accomplishments and initiatives:

Brown University—described intergenerational effects, including maternal smoking during pregnancy, that influence smoking initiation and increase the risk for nicotine addiction among adolescents.

University of California, Irvine—elucidated the neurobiological impact of nicotine, particularly on the developing brain.

University of Pennsylvania/Georgetown University—shed new light on how inherited variations in enzymes increase or decrease the likelihood of becoming addicted to nicotine or contribute to the effectiveness of smoking cessation treatments.

University of Southern California—expanded understanding of the role of cultural, ethnic, and peer influences on smoking behavior.

Yale University—identified sex differences that contribute to differential success of treatment for men and women and is developing treatments to help smokers who have had the most difficulty quitting

University of Minnesota—began developing and evaluating new smoking cessation treatments, including vaccines to prevent nicotine from reaching the brain.

University of Wisconsin—is pursuing strategies to expand access to and increase use of smoking cessation programs and identify measures that reduce the risk of relapse.



The transdermal patch, based on early NIDA research, has proven helpful to many smokers trying to overcome nicotine dependence.

Collaborating With Other Federal Agencies.

NIDA is participating in research initiatives with other NIH Institutes, including those that research allergy and infectious diseases, neurological disease and stroke, mental health, alcoholism and alcohol abuse, cancer, and child health and development. Studies funded under these initiatives will help the biomedical research and practice community better understand the links between addiction and comorbid mental and physical disorders. This research will accelerate discovery of prevention and treatment interventions for such disorders as hepatitis, HIV, mood and conduct disorders, and other problems often associated with drug abuse as cause, consequence, or both.

Working With Private Industry and Practice. Research partnerships with private pharmaceutical companies are fostering new approaches to treat drug abuse and addiction, including vaccines currently in clinical trials. Agreements negotiated with pharmaceutical companies are enabling NIDA's Medications Development Program to explore the potential of patented compounds in treating cocaine, methamphetamine, and nicotine addiction. NIDA also is working to raise private medical practitioners' awareness that they can play a critical role in improving their patients' health by being alert to the signs and symptoms of substance abuse and aware of treatment options for addiction and related medical and psychiatric problems.



Strengthening Research-Practice Partnerships.

To broaden the research-practice partnership that the CTN has initiated, NIDA has organized regional blending conferences to extend the reach of treatment research into the Nation's community treatment programs. The conferences allow clinicians and researchers to examine how to apply cutting-edge findings about drug use and addiction in clinical settings.

NIDA also supports the Substance Abuse and Mental Health Services

Administration (SAMHSA) in developing, deploying, and evaluating evidence-based treatment approaches for drug abuse in community-based clinics. These efforts bring research and practice closer together, inform development of more effective and use-ful interventions, accelerate adoption of research-tested approaches, and improve the quality of drug abuse prevention and treatment.

Improving Criminal Justice Drug Abuse Treatment Services.

The majority of the 600,000 inmates who return to their communities from prison each year have untreated substance abuse problems that can quickly lead to relapse to drug abuse and criminal behavior. Thus, NIDA has taken the lead in building a multi-agency consortium to develop integrated approaches to the treatment of incarcerated individuals with drug abuse and addictive disorders and test them at multiple sites throughout the Nation. Joining the Institute in this much-needed National Criminal Justice Drug Abuse Treatment Study to improve drug abuse treatment services for offenders are SAMHSA, the Centers for Disease Control and Prevention, and the Department of Justice. **NN**



Fostering research-clinician partnerships is a focus of Science & Practice Perspectives, NIDA's peer-reviewed journal.

Developing Effective Addiction Treatments

Pursuing New Medications

In recent years, people from all walks of life have sought treatment for addiction to powerful narcotic pain-relieving medications, such as OxyContin and Vicodin, that they have abused outside of a medical regimen. These medications share many properties with heroin, which currently ensnares more than a million people nationwide in the web of addiction. Those who become addicted to legal painkillers or street opiates now have a new medication to help them reclaim their lives. Approved by FDA in 2002, buprenorphine joins two other approved opiate treatment medications—methadone, used in long-term treatment, and the NIDA-developed opiate blocker naltrexone, used to help patients remain drug-free after they have stopped using opiates.

Buprenorphine is the first medication for opiate addiction treatment that can be prescribed by private physicians in offices and clinics. Use of this medication in mainstream medicine should help reduce the stigma still associated with drug abuse treatment, while encouraging more patients to seek treatment for addiction to heroin and other opiates. NIDA also is pursuing medications for cocaine and methamphetamine abuse and addiction, for which no medications are yet available. To fill this void, the Institute is applying the same scientific medications development methodologies that put effective opiate treatment medications into the hands of clinicians and their patients.

On one research track, clinical researchers are screening medications previously approved to treat other disorders. In these small-scale trials, several agents have appeared to weaken the addictive cycle of drug-craving, drug-seeking, and drug-taking. Among them are amantadine (currently used for Parkinson's disease), disulfiram (Antabuse), baclofen (an antispasticity agent), tiagabine and topira-

mate (antiepileptics), and modafinil (used in narcolepsy). Disulfiram and naltrexone, both effective in treating alcoholism, may fill a critical need for medications that can help cocaine-abusing individuals who also abuse alcohol. Propranolol, a medication used to lower blood pressure, may help substance abuse patients stay the course during the critical early days of treatment, by alleviating their unpleasant withdrawal symptoms. Researchers are now conducting larger, longer studies to confirm these encouraging results. Because the medications work by a variety of different mechanisms, some of which may complement each other, researchers also will examine whether they may be more effective in combination than alone. Some

may also work optimally with specific behavioral therapies.

On another track, researchers in NIDA's cocaine and methamphetamine treatment discovery programs are working to identify new chemical compounds whose pharmacological actions modulate the effects of psychostimulants on the brain and behavior. They already have shown that one compound that blocks a brain can-

nabinoid receptor can prevent animals from reinitiating cocaine use after exposure to drug-related cues and stressful events. Other compounds that curb the drug-induced flooding of the brain's reward pathways with dopamine may be able to treat addiction to all abused drugs. Still other compounds counter psychostimulants' ability to activate receptor molecules, nerve networks, and neurochemical mechanisms to create pleasure and craving.

Another NIDA initiative is focusing on new medications for treating nicotine addiction. Launched in the 1970s, NIDA's basic research in this area provided the scientific basis for nicotine replacement therapies, such as the transdermal patch, that today help many patients overcome nicotine dependence. The Institute is now pursuing several approaches to medications that could intercept





NIDA uses art cards, displayed in restaurants and other public places, to warn smokers that nicotine, like other drugs, can be addictive.

that reinforce their abuse and addiction are critical in treating drug abuse and preventing its harmful consequences. Cognitive-behavioral therapies can stand alone as front-line interventions that help many patients stop using drugs and remain drug-free. And they can increase the effectiveness of treatment medications by boosting patients' motivation to remain in treatment, take their medication as scheduled, and learn strategies to avoid relapse and lead drug-free lives. NIDA-supported research has demonstrated that combining medications, as available, with behavioral treatments is the best way to enhance success for most patients.

Over the last decade, NIDA's Behavioral Therapies Development Program established a three-stage process to develop and introduce new behavioral approaches into clinical practice, similar to that required by the Food and Drug Administration to establish the safety and efficacy

and neutralize nicotine, cocaine, and methamphetamine in the bloodstream before they can act in the brain. In one approach, vaccines containing the abused substance are linked with a larger carrier molecule and stimulate the body to produce antibodies to the drug. Another approach enhances the rate at which the body's enzymes break down the drug molecules into inactive byproducts.

Identifying Effective Behavioral Therapies

Therapies that help drug abuse patients overcome erroneous thought patterns and behaviors



of medications. Building on research that suggests avenues for developing new therapies or refining existing ones, pilot studies explore the potential of each new or refined treatment. Those showing promise are then tested in research settings in small- and large-scale clinical trials. Finally, clinical trials can be done in community settings for those therapies that demonstrate therapeutic efficacy.

NIDA behavioral therapy researchers have designed several cognitive-behavioral therapies to help methamphetamine abusers. One innovative therapy gives patients a voucher each time they submit a drug-free urine sample. Vouchers may be exchanged for goods or services that provide pleasurable, legal alternatives to drug use or, as in methadone treatment programs, for special privileges, like reducing the number of required visits to a treatment clinic. Studies show that providing vouchers for drug-free urine tests can help patients stop cocaine and methamphetamine use and remain abstinent for extended periods. Variations of voucher-based therapies that use lower cost vouchers or involve family and other community resources in treatment can be matched to the resources of treatment programs and needs of cocaine-addicted individuals.

In the last 10 years, behavioral treatments have demonstrated their potency in improving the health of diverse individuals with many types of drug abuse and other men-



Family therapies tailored to the ethnicity or race of substance-abusing teens have proven successful.

tal disorders. Proven treatments include individual cognitive-behavioral therapy, family therapies for Hispanic and African-American adolescent substance abusers, combination behavioral and medication therapies for adult smokers, and couples therapy for opiate-addicted men and

women in methadone treatment programs. The benefits of many of these treatments endure long after treatment has ended. And with individual cognitive-behavioral therapy, the benefits appear to increase over time. **NN**

Animal Studies Suggest D₃ Receptors Offer New Target for Treatment Medications

By Jill Schlabig Williams, NIDA NOTES Contributing Writer

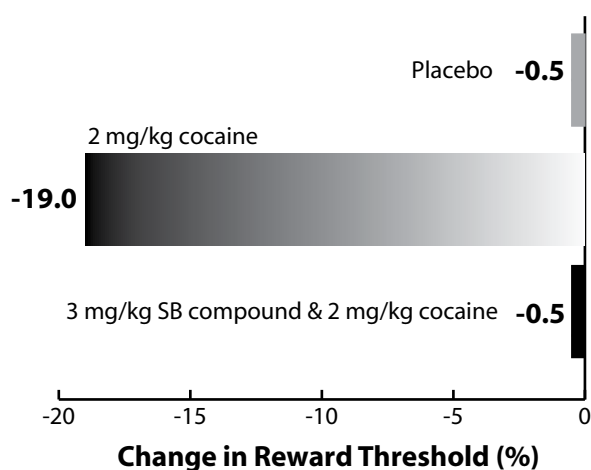
Collaboration between a NIDA scientist and a researcher from St. John's University in Jamaica, New York, has identified a chemical compound that prevents animal responses to cocaine that correspond to human drug liking, seeking, and relapse. While the compound is not suitable as a medication, the researchers believe its mechanism of action—restricting neurotransmitter access to the dopamine D₃ receptor—may provide a basis for pharmacological treatments for addiction to cocaine and other drugs.

The chemical messenger dopamine plays a critical role in networks of brain cells that trigger the rewarding feelings that result when we engage in pleasurable activities, such as eating. Drugs of abuse activate hot buttons, called receptors, on these brain cells, flooding the brain's reward pathways with dopamine and producing intense pleasure. With continued drug abuse, overstimulation of these pathways changes the brain, leading to the intense craving and uncontrollable pursuit of drugs that mark addiction.

To derail this process, research has focused on the use of agonists, compounds structurally similar to dopamine that bind to and stimulate dopamine receptors and seem to inhibit drug-seeking behavior, and antagonists, which bind to and block these receptors. Until now, researchers have tried developing a treatment medication that can counter the addictive effects of abused drugs at two different dopamine receptors, called D₁ and D₂, with little success. Potential treatment agonists that activated these receptors produced such strong stimulation that it seemed likely they themselves would be abused. And the antagonists used to block the pleasurable effects of abused drugs at these receptors produced aversive, unpleasant effects. However, recent NIDA-funded research on use of an antagonist designed to target a less-studied dopamine receptor called D₃ offers new promise. Researchers Dr. Charles Ashby, Jr., of St. John's University, and Dr. Eliot Gardner, of NIDA's Intramural Research Program, note that D₃ appears to play a major role in addiction and may be the elusive target for medications that could help control addictive behavior.

Scientists have identified five subtypes of dopamine receptors, each with distinct properties and each found in varying densities in different areas of the brain. To date, most research has focused on the roles of the D₁ and D₂ receptors, which occur in higher densities and more places

D₃ Receptor Antagonist Blocks Cocaine Reward in Rats



Cocaine exposure lowered by 19 percent rats' reward threshold, the amount of current needed to motivate an animal to push a lever to activate electrical stimulation of its brain reward system. When rats were given the D₃ antagonist before being given cocaine, however, their reward threshold remained the same as when they were given placebo.

in the brain than do D₃ receptors. Nevertheless, several characteristics of the D₃ receptor suggested that medications that interact with it may have promise as treatments for cocaine addiction. D₃ receptors are mainly concentrated in the brain's reward pathway. In addition, dopamine is attracted more strongly to the D₃ receptors than to other receptors. Yet researchers found that D₃ agonists caused rats to resume drug-seeking behavior more quickly after a period of abstinence. This reaction suggested that a compound capable of selectively blocking this receptor—an antagonist—could be important in developing a medication to reduce or block craving.

The D₃ antagonist compound used in the Ashby-Gardner studies, called SB-277011-A, is highly selective, with an 80- to 100-fold preference for D₃ over D₂ receptors and 66 other receptors, enzymes, and ion channels. When the compound was first developed in 1997, Drs. Ashby and

Gardner saw its potential. “Until then, study of the D₃ receptor was hampered because the available compounds antagonized D₂ as well as D₃ receptors to some extent, making it difficult to sort out which was responsible for the observed effects. As a result, research on the D₃ receptor and compounds that affect it had yielded inconsistent and contradictory results,” explains Dr. Ashby. “We knew this compound and its unambiguous selectivity for D₃ receptors would allow us to test the role of these receptors, while offering promise as a treatment for addiction.”

Drs. Ashby and Gardner performed three types of animal experiments. “Each experiment used the D₃ antagonist to focus on a unique aspect of addiction, and all three yielded promising results,” says Dr. Ashby. “Antagonizing the D₃ receptor appears to weaken cocaine’s rewarding effects, reduce cocaine-induced conditioned place preference, and block reinstatement of drug-seeking behavior. And the compound we were testing was not found to be rewarding or aversive.”

Cocaine’s Rewarding Effects

In the first set of studies, researchers used brain stimulation reward experiments to measure the direct rewarding properties of cocaine. This type of experiment is thought to produce the closest equivalent in animals to the cocaine-induced subjective high experienced by humans. The researchers implanted brain stimulation electrodes in rats and trained the animals to press a lever to self-administer electrical stimulation that produced feelings of pleasure or euphoria. Baseline reward thresholds, the amount of current below which the animal no longer finds the stimu-

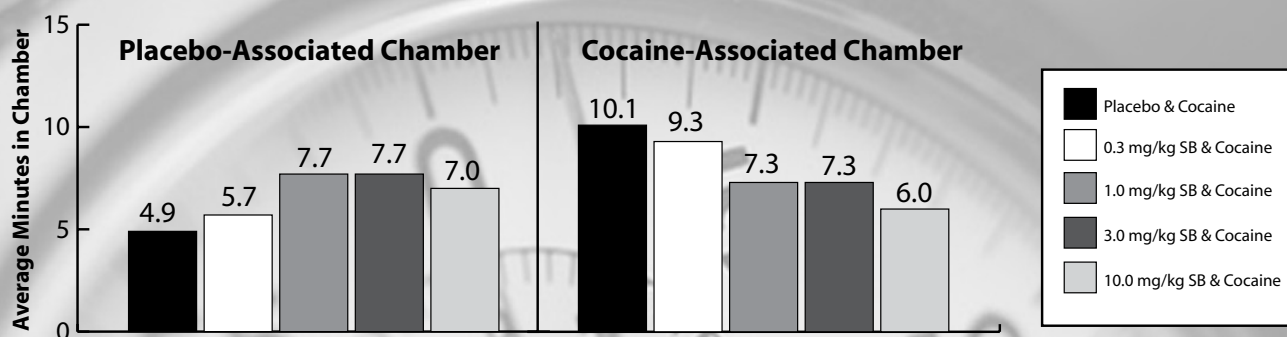
lation rewarding enough to press the lever, were determined for each animal. Drugs of abuse, which activate the same neurons in the brain’s reward system as the electrical current, increase the amount of pleasure obtained from a given amount of current and therefore decrease the reward threshold. The difference between baseline reward threshold and the reward threshold after administration of a drug gives a measure of the rewarding potency of the drug being tested.

After establishing the rats’ baseline reward thresholds, researchers injected the animals with placebo, 2 mg/kg cocaine, or 3 mg/kg SB compound followed by 2 mg/kg cocaine; researchers then retested the rats. As expected, the reward threshold of animals injected with placebo remained unchanged; those injected with cocaine had an average 19-percent decrease in their reward thresholds. Rats pretreated with the D₃ antagonist and then given cocaine had no change in their reward thresholds, indicating that the antagonist completely abolished the enhancing effect of cocaine on brain reward.

Cocaine-Seeking Behavior

The second set of experiments used conditioned place preference, aiming to measure cocaine-seeking behavior evoked by environmental cues associated with cocaine. The experiments involved providing rats one of five pretreatments—placebo or varying doses of the SB compound—and then confining them to one chamber of a two-room cage. The rats were subsequently given cocaine and confined to the other chamber. Each chamber had distinct visual and tactile furnishings. Rats were then allowed to freely explore

D₃ Receptor Antagonist Blocks Rats’ Incentive to Seek Cocaine



Rats were given placebo and confined to one chamber of a two-chamber cage, then given cocaine and confined to the other chamber. They were then allowed to roam throughout the cage for 15 minutes, with researchers measuring the time spent in each chamber. This exercise was repeated with four other groups of rats, which were given either 0.3 mg/kg, 1 mg/kg, 3 mg/kg, or 10 mg/kg D₃ antagonist (SB compound) and then cocaine. Rats treated with the SB compound before receiving cocaine spent significantly less time in the cocaine-associated chamber than rats pretreated with placebo.

the entire cage for 15 minutes, while researchers measured their time in each chamber.

Rats given placebo and then cocaine spent roughly two thirds of their time in the chamber they associated with cocaine. However, rats pretreated with the D₃ antagonist (SB compound) spent, on average, less time in the cocaine-associated chamber, with the minutes spent in that chamber decreasing as the D₃ antagonist dose increased from 0.3 mg/kg to 1 mg/kg, 3 mg/kg, and up to 10 mg/kg. Rats pretreated with the highest dose of the D₃ antagonist spent about 40 percent fewer minutes in the cocaine-associated chamber than did rats in the placebo-cocaine group. The results indicate that the D₃ antagonist blocked the rats' motivation to seek out cocaine, eliminating their acquisition and expression of cocaine-induced conditioned preference.

Reinstatement of Drug Seeking

The final set of experiments focused on cocaine self-administration and reinstatement. The researchers implanted an intravenous catheter in the rat's external jugular vein and trained the animal to self-administer cocaine by pressing a lever. The daily 3-hour sessions continued until the rat was self-administering consistent amounts of the drug every day. The researchers then phased out the lever-pressing behavior by substituting saline for the cocaine; since pressing the lever no longer resulted in cocaine, the rats lost interest and pushed the lever much less often. At this point, the researchers gave rats that had been pretreated with placebo or the SB compound a priming dose of cocaine (1 mg/kg) normally sufficient to trigger reinstatement of the drug-seeking, lever-pressing behavior. The rats returned to the lever, and the researchers counted how many times they pressed it.

On the day before they were given the priming dose of cocaine, rats pressed the active lever an average of 7.7 times. After receiving the priming dose, the rats pretreated with placebo pressed the lever an average of 38.8 times, while rats pretreated with 3, 6, or 12 mg/kg of the D₃ antagonist pressed the lever an average of 39.0, 18.6, and 14.2 times, respectively. Pretreatment with the D₃ antagonist thus produced a dose-related weakening of cocaine-triggered resumption of the drug-seeking behavior.

Future of D₃ Antagonist Research

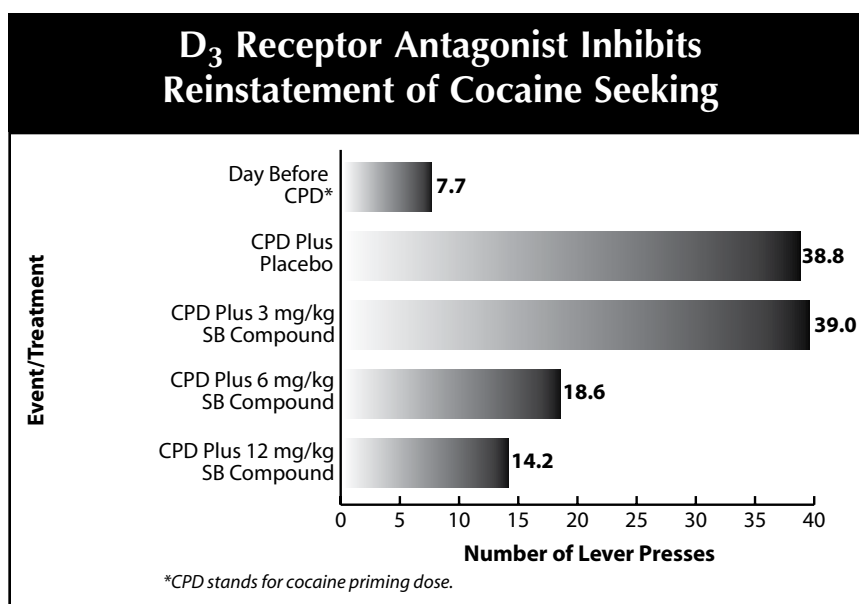
The researchers are optimistic about the future of this line of research. "The SB compound has jumped through many hoops already," says Dr. Ashby. "It's

been shown in our studies and other studies to block cue-induced, drug-induced, and stress-induced relapse to cocaine-seeking behavior, and acquisition and expression of heroin-induced conditioned place preference. It is neither rewarding nor aversive and has been found to work on cocaine, heroin, and nicotine. We've seen no significant adverse effects of the compound in animals. We think antagonizing the D₃ receptor represents a breakthrough for addiction treatment."

"In more than 35 years in the field, this D₃ antagonist research is the most promising thing I have ever seen," Dr. Gardner says. "No one else has assembled such a variety of animal evidence showing that acute administration of a compound so profoundly modifies the addictive properties of cocaine as this selective D₃ antagonist."

Both Drs. Ashby and Gardner are quick to note, however, that much work lies ahead. "We don't know if these results will hold up in long-term studies," says Dr. Gardner. "We think the reason this compound is successful in animal studies is because of its D₃ antagonist action. To verify this, we still need to develop other, chemically different D₃ antagonists and redo all the tests. If we obtain the same results with these other D₃ antagonists, then we'll be more comfortable that we are on the right track and that D₃ receptor antagonism is truly responsible for our findings."

More animal experiments are planned to focus on other drugs of abuse and other animal paradigms, such as progressive ratio studies that measure a drug's motivational potency. Studies with chronic administration and with other mammalian species also will be needed, as will



After receiving a priming dose of cocaine, rats pretreated with placebo resumed cocaine-seeking behavior, pressing a lever to self-administer cocaine. However, rats pretreated with the D₃ antagonist (SB compound) pressed the lever fewer times as the SB compound dose increased.

toxicology studies. The human pharmacokinetics of the compounds also will have to be improved; for instance, the current compound has a very short half-life, lasting only about 30 minutes in primates.

“Almost without fail, people I’ve spoken with who are addicted to drugs express a strong desire for clinically effective anticraving, antirelapse medication,” says Dr. Gardner. “We hope this research takes us in that direction.”

Source

- Vorel, S.R.; Ashby, C.R., Jr.; Paul, M.; Liu, X.; Hayes, R.; Hagan, J.J.; Middlemiss, D.N.; Stemp, G.; Gardner, E.L. Dopamine D₃ receptor antagonism inhibits cocaine-seeking and cocaine-enhanced brain reward in rats. *Journal of Neuroscience* 22(21):9595-9603, 2002. **NN**

Network Therapy Expands Treatment Capabilities Of Small Practice Providers

By Patrick Zickler, NIDA NOTES Staff Writer

NIDA-supported researchers have found that clinicians without access to the resources of a comprehensive substance abuse program can treat cocaine abuse with “network therapy,” a treatment approach that combines individual therapy and the involvement of patients’ friends or family members. The patient completion rate—a key measure of the likelihood that patients will remain drug free—is comparable to that of other outpatient treatment approaches, the researchers say.

Network therapy was developed through NIDA’s Behavioral Therapies Development Program by Dr. Marc Galanter and his colleagues at the New York University School of Medicine in New York City. The treatment combines cognitive-behavioral therapy, which enables patients to identify and develop strategies to avoid or cope with circumstances that lead to their drug use, with network sessions that include the patient and one or more “network members”—family members or peers who are not substance abusers.

“Network therapy expands the practitioner’s capability to treat cocaine abuse by enlisting family and peer support to provide the reinforcement necessary for the patient’s success,” says Dr. Galanter. “Physicians in small practices do not have the benefits offered by a large clinical environment, such as social workers, multidisciplinary psychiatric staff, or the opportunity to schedule nightly group meetings. This approach helps overcome those limitations.”

The researchers trained 28 psychiatry residents to provide network therapy. Training involved classroom seminars and video presentations based on a 122-page manual. The residents then treated 47 patients who had applied for cocaine abuse treatment and had no other substance abuse or psychiatric disorder.

The patients (mean age 35 years, 85 percent male, 62 percent white) paid \$20 per session over a 24-week sequence of twice-weekly individual therapy sessions. Network sessions were held weekly for the first month and monthly thereafter. Twelve patients dropped out of the program after the first week. Of the 35 who remained beyond the first week, nearly half (17) completed the full 24-week course of treatment, a completion rate comparable to those in other outpatient treatment programs.

Treatment success for each participant was based on two measures: the proportion of drug-free weekly urine tests



Dr. Marc Galanter, of New York University School of Medicine, reviews a training tape to be shown to clinicians learning network therapy. Developed through NIDA’s Behavioral Therapies Development Program, network therapy combines individual cognitive-behavioral therapy with sessions that include the patient and members of his or her network—family members or peers.

and the participant’s drug-free status for the last three tests. Overall, 73 percent of tests throughout treatment were drug free; 20 participants (43 percent of the entire group) were drug free the last 3 weeks of treatment. Success was most likely among patients who involved network members and remained in treatment longest.

“The network sessions involved training network members to provide a supportive environment for abstinence to help patients adhere to behavioral strategies, such as avoiding situations that might trigger drug use,” Dr. Galanter explains. “Interestingly, it was the number of network sessions—not the number of individual sessions—that most closely correlated with a good outcome. This suggests the central role of involvement with network members in shaping outcome.”

Dr. Dorynne Czechowicz of NIDA’s Division of Treatment Research and Development says that the involvement of young doctors in the delivery of network therapy represents a significant additional accomplishment of this research. “The recent approval of buprenorphine for office-based treatment of opiate addiction represents a first step in the movement of drug abuse treatment out

of specialized facilities and into the more routine world of health care,” she says. “Training young doctors to deliver therapy is a crucial step in getting general practitioners involved in drug abuse treatment, and treatments such as network therapy can help accelerate that movement.”

Dr. Galanter is now conducting a study of the effectiveness of network therapy in combination with the administration of buprenorphine in treating heroin addiction. “There is a need for training in psychosocial approaches to drug abuse treatment that are applicable to a practitioner’s office, both as a stand-alone option and in combination with pharmacotherapy,” Dr. Galanter says. “Our findings

in the use of network therapy in treating cocaine addiction are promising. Results so far suggest that network therapy may also be a valuable, easily delivered approach to support buprenorphine treatment in an office setting.”

Source

- Galanter, M.D.; Dermatis, H.; Keller, D.; and Trujillo, M. Network therapy for cocaine abuse: Use of family and peer supports. *American Journal on Addictions* 11(2):161-166, 2002. **NN**

A Double Dose of Research for Patients Addicted to Both Drugs and Alcohol

By NIDA Director Nora D. Volkow, M.D.

Addiction researchers and treatment professionals have long known that drug addiction and alcoholism are strongly linked. In the last decade, research has broadened our understanding of many shared neurobiological and behavioral mechanisms that underpin the two disorders. Yet, while two in five substance abuse treatment patients abuse both drugs and alcohol, the treatment they are likely to receive will target only one disorder. A lack of science-based information on concurrent treatment of drug and alcohol abuse limits the ability of treatment professionals to provide the comprehensive treatment these patients need.

Recent research suggests that some medications developed to treat drug or alcohol abuse may be useful for treating both problems. This information, along with our increased understanding of the underlying factors that drive drug and alcohol abuse, provides a strong rationale for a coordinated



according to the National Household Survey on Drug Abuse. In fact, the more heavily someone abused alcohol, the more likely he or she was to use illicit drugs, the survey found. In 2001, nearly two of every three American teenagers, ages 12 to 17, who engaged in frequent drinking binges also abused drugs. In comparison, only 1 in 20 young people who didn't drink at all used drugs.

The substantial portion of drug- and alcohol-abusing patients in community treatment programs provides additional evidence of the need for science-based information on treating dual addiction. Patients who abuse both drugs and

alcohol accounted for more than 42 percent of admissions to substance abuse treatment facilities reported by State agencies in 2000, the last year for which these data are published. Alcohol abuse is even more likely among patients who abuse certain drugs, such as cocaine, methamphetamine, and marijuana. For example, more than half of cocaine-abusing patients who entered treatment in 2000 also abused alcohol.

Recent research suggests that some medications developed to treat either drug or alcohol abuse may be useful in treating co-occurring substance abuse.

research effort to meet the critical need for treatments for people suffering from both disorders. Toward that end, NIDA and the National Institute on Alcohol Abuse and Alcoholism (NIAAA) have issued a joint program announcement (PAS-03-029) to spur both drug and alcohol abuse researchers to investigate all aspects of pharmacological treatment for dually addicted patients.

Coordinated research on dually addicted patients will address the needs of the overwhelming number of Americans who abuse both alcohol and illicit drugs. More than 2.4 million of the 5.6 million people who abused illicit drugs in 2001 also abused alcohol,

We aim to generate a broad spectrum of useful clinical information about appropriate sequencing or combining of medications and behavioral therapies, possible drug interactions that could affect optimal dosages, and unique requirements of specific groups of dually addicted patients...

To develop effective treatments for patients who abuse both drugs and alcohol, we need to understand why so many people do so. Part of the answer probably has to

do with genes—underlying genetic variations that may play a role in common brain mechanisms that fuel both disorders. NIDA-supported brain imaging studies conducted at Brookhaven National Laboratory in Upton, New York, have documented similarities in the structure and function of the brains of alcoholics and chronic cocaine abusers that appear to be implicated in the abuse of both substances. Individuals with either disorder have low levels of dopamine D₂ receptors in the brain's reward pathways that may impair their capacity to derive pleasure from normally rewarding activities. This deficit may make them more vulnerable to the rewarding effects of alcohol and cocaine.

Dually addicted individuals also may combine alcohol and illicit drugs because of interactions between abused substances in the body. Because both drugs and alcohol activate brain areas involved in reward, combining substances may increase these effects. Other alcohol-drug interactions may counter unpleasant effects that often accompany or follow substance abuse. Clinical reports suggest that cocaethylene, a combined cocaine-alcohol metabolite that is formed in the body following concurrent alcohol and cocaine use, appears to reduce the anxiety that can accompany cocaine use. Recent research in rats confirms that cocaethylene plasma levels remain high as cocaine levels fall, producing a delayed, relatively long-lasting rewarding

effect that may counter the aversive effect induced when cocaine plasma levels recede.

While the perceived benefits of combining alcohol and drugs may play a big part in the high percentages of people who do so, the addictive effects and harmful consequences of both substances increase when they are used together. Dually addicted patients are more likely to drop out of treatment and have poorer results than patients who abuse only one substance. However, since most studies on treating drug and alcohol abuse have examined these disorders separately, drug and alcohol treatment counselors now have little science-based information on which to base their treatment of these patients.

The joint NIDA-NIAAA program announcement addresses this critical need for effective approaches to treating dually addicted patients. Our research partnership seeks studies that will evaluate the efficacy of established drug and alcohol treatment medications and novel pharmacological agents in patients with concurrent addictions. We aim to generate a broad spectrum of useful clinical information about appropriate sequencing or combining of medications and behavioral therapies in dually addicted patients, possible drug interactions that could affect optimal dosages, and unique requirements of specific groups of patients, such as minorities, the elderly, and adolescents.

Drug and alcohol abuse wreak incalculable damage on individuals, families, and communities. When they occur together, these disorders double the challenge to researchers and treatment providers. Now, NIDA and NIAAA have launched a concerted scientific response to address these challenges. Ultimately, this expanded research will fuel the development of new treatments that will enable substance abuse treatment programs to more effectively meet the needs of the many patients who abuse both alcohol and illicit drugs. **NN**

The joint NIDA-NIAAA program announcement addresses the critical need for effective approaches to treating dually addicted patients.

Treating Adolescent Substance Abuse by Addressing Family Interactions

Brief Strategic Family Therapy (BSFT) is described in the latest addition to the *Therapy Manuals for Drug Addiction* series. The short-term intervention is used to treat adolescent drug use that occurs along with other problem behaviors. This therapy focuses on an adolescent's drug use within the context of family dynamics.

The BSFT manual introduces counselors to concepts they need to understand the family as a vital context within which adolescent drug abuse occurs. It also describes strategies for creating a therapeutic relationship with families, assessing and diagnosing maladaptive patterns of family interactions, and changing family interaction patterns from maladaptive to adaptive.

BSFT can be adapted to a range of family situations and used in a variety of service settings—such as mental health clinics, drug abuse treatment programs, and other social service settings. It also can be delivered in various ways, such as on an outpatient basis or in combination with residential or day treatment. Treatment lasts 8 to 24 sessions, depending on the severity of the problem.

In addition to targeting an adolescent's conduct problems at home and at school, BSFT addresses oppositional, aggressive, violent, or risky sexual behavior; association with antisocial peers; and delinquency. Family dynamics are a key focus of this therapy.

Over 25 years of extensive evaluation has found BSFT to be effective in treating adolescent drug abuse, conduct problems, association with antisocial peers, and impaired family functioning. It has been shown to be particularly successful with cultural groups that emphasize family and interpersonal relationships. BSFT has not been tested with adult addicts and is not considered a treatment for adult addiction.

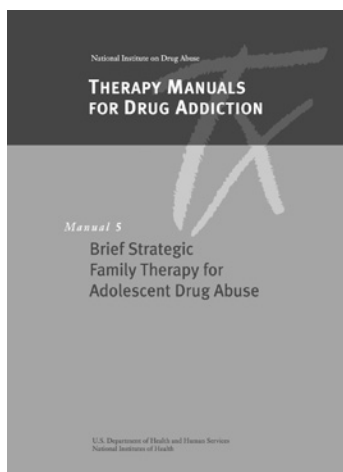
The upcoming manual and the series of which it is a part exemplify NIDA's commitment to applying basic research findings to treatment needs. In addition to describing scientifically based therapies for addiction, the five manuals provide guidance on content for counseling sessions and

effective counseling techniques. Audiences include drug abuse treatment practitioners, mental health professionals, and others involved in treating drug abuse and addiction.

Therapy Manuals Offer a Range of Treatment Strategies

The four earlier therapy manuals can be downloaded from NIDA's Web site, www.drugabuse.gov, or ordered through the National Clearinghouse for Alcohol and Drug Information, <http://ncadi.samhsa.gov/>. The *Brief Strategic Family Therapy* manual also will soon be available from these sources.

- *A Cognitive-Behavioral Approach: Treating Cocaine Addiction* (Manual 1) describes cognitive-behavioral coping skills treatment, a short-term, focused approach to helping cocaine-dependent individuals abstain from cocaine and other drugs.
- *A Community Reinforcement Plus Vouchers Approach: Treating Cocaine Addiction* (Manual 2) integrates a community reinforcement approach with an incentive program that uses vouchers. Patients earn points to redeem for retail items by remaining in treatment and abstaining from cocaine.
- *An Individual Counseling Approach to Treat Cocaine Addiction: The Collaborative Cocaine Treatment Study Model* (Manual 3) presents a guide for the individual treatment of cocaine addiction that emphasizes an individual's physical, emotional, spiritual, and interpersonal needs in supporting recovery.
- *Drug Counseling for Cocaine Addiction: The Collaborative Cocaine Treatment Study Model* (Manual 4) describes the Group Drug Counseling (GDC) model developed for the Collaborative Cocaine Treatment Study (CCTS), a multisite clinical trial. The study found the combination of GDC and individual drug counseling to be more effective than GDC alone or the combination of GDC and psychotherapy. **NN**



Family-Based Treatment Programs Can Reduce Adolescent Drug Abuse

By Patrick Zickler, *NIDA NOTES* Staff Writer

Many factors influence adolescent drug abuse. Peer relationships; family, school, and neighborhood environments; and social or cultural norms can each act as protective factors or can put adolescents at increased risk. NIDA-supported researchers are developing and evaluating a variety of treatments designed to address the range of influences that play a role in adolescent drug abuse. In a study that compared three treatment approaches, researchers have found that Multidimensional Family Therapy (MDFT), which involves individual therapy and family therapy, produced better treatment outcomes than did Adolescent Group Therapy (AGT) or Multifamily Educational Intervention (MEI), a treatment delivered in sessions involving more than one family.

Dr. Howard Liddle at the University of Miami School of Medicine and colleagues at the University of Pennsylvania in Philadelphia, the University of Washington in Seattle, and Families First, a treatment center in Stockton, California, evaluated the treatment programs in a study involving 152 adolescents who had been referred to treatment through the juvenile justice system. The participants (average age 15.9 years, 80 percent male) came from single-parent families (48 percent), two-parent families (31 percent), and stepfamilies (21 percent) and had been using drugs for an average of 2.5 years; 51 percent were polydrug users, 49 percent marijuana and alcohol users.

Participants were randomly assigned to one of the treatment programs, which were administered in community clinics in weekly sessions over a period of 5 to 6 months.

Before treatment began, the researchers evaluated each participant's drug use, school performance, problem behavior (acting-out behavior measured by a widely used assessment scale), and family functioning (measured by the Global Health Pathology Scale). The same characteristics were measured at the end of treatment and at followup evaluations 6 months and 12 months after treatment ended.

Overall, the adolescents showed reductions in drug use after all three treatment programs, but the improvements were greatest for participants who received MDFT. At the end of treatment, 42 percent of MDFT, 25 percent of AGT, and 22 percent of MEI participants had decreased their drug use. Drug use declined further in the 12 months

Multidimensional Family Therapy Reduces Youth Drug Use, Improves School Performance and Family Interaction

	Start of Treatment	End of Treatment	12-Month Followup
Drug Use, Past 30 days^a			
1 (no use) to 15 (marijuana use daily and other drugs used more than twice per week)			
MDFT ^b	9.89	4.79	4.25
AGT	8.83	7.33	5.08
MEI	10.03	7.26	7.26
Academic Performance^a			
Grade point average from 1 (D) to 4 (A)			
MDFT	1.77	2.56	2.62
AGT	1.85	2.44	2.26
MEI	1.98	2.05	1.92
Family Function^a			
1 (optimal) to 10 (severely dysfunctional)			
MDFT	6.15	5.18	4.70
AGT	6.00	5.67	5.83
MEI	4.31	4.77	5.35

^a Average of all patients.

^bMDFT = Multidimensional Family Therapy; AGT = Adolescent Group Therapy; MEI = Multifamily Educational Intervention.

Multidimensional Family Therapy, which involves individual therapy and family therapy, produced better treatment outcomes for teenagers than did Adolescent Group Therapy or Multifamily Educational Intervention, a treatment delivered in sessions involving more than one family.

following treatment, with MDFT associated with the greatest reduction. Participants in MDFT also showed greater improvement in family functioning and academic performance than did adolescents who received AGT or MEI treatment.

“There was an overall pattern of improvement for each of the treatments, but family-based therapy stands out in its success in this study,” Dr. Liddle says. “Those receiving MDFT showed the most improvement in drug use and academic performance, followed by participants who received AGT, then those receiving MEI.”

Improvement in family function was most notable in MDFT participants, Dr. Liddle says. “The MDFT families moved from assessments of ‘behaviorally incompetent’ to the ‘competent’ range, while AGT families showed no change, and MEI families deteriorated on the family functioning scales.”

Participants in MDFT were less likely than those in other programs to drop out of treatment—70 percent of those assigned to MDFT completed treatment, compared with 66 percent of participants in MEI and 52 percent in AGT.

Each program provided improvement in one or more outcomes measured in the study, but involvement of family members was associated with the best overall progress. “Given the pattern of results, it seems reasonable to conclude that a simultaneous focus on the family and the individual adolescent is an important ingredient for successful treatment of adolescent drug abuse,” Dr. Liddle says.

Source

- Liddle, H.A., et al. Multidimensional family therapy for adolescent drug abuse: Results of a randomized clinical trial. *American Journal of Drug and Alcohol Abuse* 27(4):651-687, 2001. **NN**

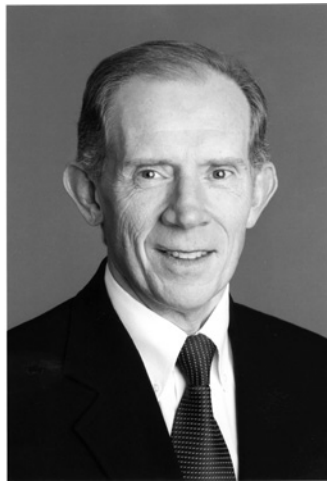
New Insights Into Relapse

By NIDA Acting Director Glen R. Hanson, Ph.D., D.D.S.

Drug addiction is a chronic relapsing disorder. As when patients in treatment for hypertension or asthma temporarily lose control, relapse to drug abuse does not mean treatment does not work, or the patient is not making an effort, or he or she will never have a productive life with long-term freedom from disease. Nevertheless, relapse is perhaps the most frustrating and demoralizing feature of drug addiction, for those who have it and those who would help them.

Clinical observation and research tell us that three types of stimulus can trigger intense drug craving, leading to renewed abuse:

- **Priming:** “Just one” exposure to the formerly abused substance—be it a cigarette, a drink, or an illegal drug—can precipitate rapid resumption of abuse at previously established levels or greater.
- **Environmental cues (people, places, or things associated with past drug use):** One vivid illustration of the power of such cues is a negative one: A small percentage of American service personnel became addicted to heroin while overseas during the Vietnam War. When they were removed from that environment, the great majority, after detoxification, reported no further problems with opiates.
- **Stress:** Both acute and chronic stress can contribute to the establishment, maintenance, and resumption of drug abuse. Patients and treatment providers alike point to stress as the most common cause of relapse. The impact of stress recently was highlighted when researchers documented increased rates of smoking and alcohol consumption by New Yorkers after the September 11, 2001 attacks.



New research findings appear to shed light on one of the deepest mysteries involving drug relapse: What accounts for the extraordinary persistence of drug cravings?

Our knowledge of relapse is incorporated in science-based drug treatments. In cognitive-behavioral therapy, for example, patients learn to confront the consequences of their drug use, recognize the environmental cues and potentially stressful situations that trigger strong drug cravings, and develop strategies to steer clear or respond without relapsing. Recent research has shown that patients who benefit from cognitive-behavioral therapy may even show further improvement after treatment has ended and with passing time.

Science-based medical treatments buffer patients against the craving that leads to relapse. Methadone and other opioid agonist agents block the euphoric effects of opioids and stabilize brain processes whose disruption is linked to craving. Naltrexone, an opioid antagonist, blocks opioid-induced euphoria and counters opioid craving with an aversive effect. Disulfiram (Antabuse) is used to treat alcohol abuse, and it is currently being tested to determine whether it also can offset cocaine craving. Antianxiety agents are prescribed to moderate stress.

New research findings appear to shed light on one of the deepest mysteries involving drug relapse: We know that former abusers of addictive drugs remain vulnerable to powerful drug cravings for months or years after establishing abstinence. What accounts for the extraordinary persistence of drug cravings?

Scientists have known for some time that addictive drugs hyperactivate key brain circuits that provide pleasure and are closely linked to motivation and memory. Research also has shown that drugs change brain cells in these circuits in numerous ways, some of which might be linked to craving. However, these changes generally last only as long as a drug is actually present, or a little longer. To explain

how craving can recur after long abstinence, researchers need to show that the drugs change the cells in ways that change back slowly or not at all.

The natural place to look for long-lasting drug-induced alterations is in the same circuits that produce short-term effects. Key cells in these circuits are located in an area called the midbrain; they manufacture a chemical called dopamine and release it in a nearby area called the nucleus accumbens, where it produces powerful mood effects.

During the past 3 years, research teams at Yale and Texas Southwestern Universities demonstrated that repeated exposure to cocaine produces alterations in gene activity in the nucleus accumbens that can persist for weeks. Last year, researchers at the University of Michigan showed that cocaine self-administration changes the actual shape of these neurons—a change that is long-lasting or even permanent. Moreover, its specific nature—a proliferation

of signal receptors—might be expected to contribute to craving by heightening the cells' general reactivity.

Further research will tell whether these changes are critically important to long-term vulnerability to drug craving, or whether they play a relatively minor role. The studies were conducted with laboratory animals and cocaine, and we need to find out whether they also apply in humans and with other drugs. Although uncertainties remain, these new results provide powerful confirmation of the neurobiological and chronic nature of drug addiction, evidenced at still more fundamental levels of brain cell operation. The studies also demonstrate the power of new neuroscience tools to elucidate the underlying causes of drug abuse. Ultimately, we need approaches this powerful to gain the understanding necessary to solve the mysteries of craving and generate treatments that help all patients move beyond the reach of relapse. **NN**

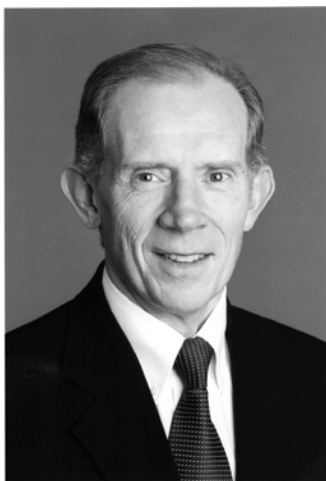
In Drug Abuse, Gender Matters

By NIDA Acting Director Glen R. Hanson, Ph.D., D.D.S.

Recent decades have seen a marked increase in awareness of the importance of gender in medical treatment and research. In the complex field of drug abuse research, scientists have helped us understand that there are genetic, physiological, psychosocial, and environmental dimensions to drug abuse and addiction. Male and female differences in any of these dimensions can give rise to gender differences in the causes, effects, and consequences of drug abuse. Researchers and clinicians have developed a repertoire of effective treatment and prevention principles that can now be enhanced through their adaptation for the differing needs of men and women and boys and girls.

NIDA's National Drug Abuse Treatment Clinical Trials Network adheres to the overall National Institutes of Health requirement for analysis of data by gender and supports gender-specific protocol development. NIDA recently issued a Program Announcement for support of dissertation research in five areas, one of which is women and gender. A new Program Announcement on Women and Gender Differences will be issued soon to fund research specifically in the areas of epidemiology, prevention, and treatment. These efforts will build on NIDA-sponsored research that has established that important gender effects exist in biological and behavioral responses to drugs, risk for drug abuse, and treatment response.

Response to drugs: The neurobiological basis of drug abuse and addiction is essentially the same, regardless of the drug taken or the person taking it. Still, males and females may differ in their biological and behavioral responses to drugs. Laboratory studies have revealed sex-related differences in the ways that male and female animals metabolize drugs, the amount of drug they will self-administer, how soon after their first exposure they begin to administer drugs, and their vulnerability to relapse



Researchers and clinicians have developed a repertoire of effective treatment and prevention principles that can now be enhanced through their adaptation for the differing needs of men and women and boys and girls.

after abstinence. Preliminary results from studies of human drug abusers appear to be consistent with the findings from animal studies of gender differences in the patterns and the biological impact of drug use. For example, women typically progress from first use of cocaine, heroin, or marijuana to dependence more quickly than men. Additionally, cocaine-induced cognitive impairments and risk for stroke have been found to be more severe in men than in women.

Risk for drug abuse: While risk factors related to drug abuse vulnerability in males and females largely overlap, a variety of differences exist. Depression is much more common among women than men in the general public. This gender difference is much less pronounced among drug abusers. Possible explanations are that depression is a more potent risk factor for drug abuse among men than among women, or that drug abuse itself is more likely to cause depression among men

than among women. Other risk factors that appear to be stronger for one gender than the other include conduct disorders, which correlate more with drug abuse by adolescent females, and aggression, which correlates with drug abuse by adolescent males.

Along with these differences, studies of gender and risk have revealed an unexpected and important similarity between males and females. Most experts long assumed that females were less attracted to or more wary of drug abuse than were males. That seemed a straightforward conclusion based on the fact that the percentage of women who abuse drugs is lower than the percentage of men who abuse drugs. However, the conclusion turns out to be not true. A recent study found that the lower rate of drug abuse for females is largely a matter of opportunity.

(See “Gender Differences in Prevalence of Drug Abuse,” *NIDA NOTES*, Vol. 15, No 4). During the youthful ages when most drug abuse initiation occurs, more boys than girls receive offers of drugs. When drug offers are made, both genders are equally likely to accept. Once having accepted, males and females generally are equally likely to become dependent. This underscores the importance of drug refusal skills in prevention efforts with both genders.

Although the focus on gender is relatively new in drug abuse science, we already know that gender’s impact is far reaching and complex.

Response to treatment: Success in drug treatment is directly associated with the length of time spent in treatment: The more time in treatment, the better the outcome. Science-based drug treatments are equally effective for men and women, but women often spend less time than men in treatment. In part, this could reflect differences in social and economic circumstances. Women entering treatment are more likely than men to be custodial parents and to have fewer economic resources; they are less likely than men to have graduated from high school, to be employed, or to have sufficient supportive social networks. Studies also indicate that males and females tend to relapse to drug use for different reasons. For example, among men relapse is more likely to be

associated with anxiety and positive feelings, while among women depression and negative feelings appear to be more common triggers. All these differences suggest that it may be possible to enhance the effectiveness of treatment by tailoring it for the patient’s gender.

The area of nicotine addiction is one in which our understanding of gender effects is relatively advanced, although still far from complete. Research has shown that different aspects of smoking more strongly influence addiction to nicotine in men and women. For men, the compulsion to smoke is driven more strongly by nicotine’s pharmacological effects on the brain, while women’s addiction owes more to the visual, tactile, taste, and olfactory sensations involved in smoking. Because of these differences, men tend to get more relief overall from nicotine replacement therapy, and women who use nicotine replacement do better with nicotine inhalers than the nicotine patch. Recent NIDA research also suggests that women can increase their chances for quitting by timing their attempt to coincide with the first half of their menstrual cycles, since nicotine craving and withdrawal symptoms are generally more severe during the second half of their cycles.

Although the focus on gender is relatively new in drug abuse science, we already know that gender’s impact is far reaching and complex. A comprehensive and detailed picture of gender-related effects can lead to improvements in treatment and prevention efforts that bring us closer to the goal of individualized interventions that best meet the distinct needs of each patient. When it comes to reducing the tremendous burden of drug abuse and addiction, gender most certainly matters. **NN**

Adolescent Treatment Programs Reduce Drug Abuse, Produce Other Improvements

By Kimberly R. Martin, *NIDA NOTES* Contributing Writer

In the first large-scale study designed to evaluate drug abuse treatment outcomes among adolescents in age-specific treatment programs, NIDA-supported researchers have found that longer stays in these treatment programs can effectively decrease drug and alcohol use and criminal activity as well as improve school performance and psychological adjustment.

The study, part of NIDA's ongoing Drug Abuse Treatment Outcome Studies for Adolescents (DATOS-A), analyzed data from 23 community-based adolescent treatment programs that addressed peer relationships, educational concerns, and family issues such as parent-child relationships and parental substance abuse. Successful elements of adult treatment programs, such as participation in group therapy and participation in a 12-step program, were also included in treatment plans.

"The results of this study are particularly impressive in light of the fact that the adolescents had multiple problems," says Dr. Christine Grella of the University of California, Los Angeles (UCLA), Drug Abuse Research Center, one of the study's investigators. "Although this is also typical of many adults in treatment, timely resolution of these problems is even more critical for adolescents. These young people are in the process of developing values, making lifestyle decisions, and preparing to assume adult roles and responsibilities, such as family and work; whereas when many adults enter treatment, they have completed this process."

Treatment Programs Varied

Dr. Yih-Ing Hser, also of UCLA, led the research team that evaluated the treatment outcomes for 1,167 adolescents, age 11 to 18, who were admitted to one of the treatment programs between 1993 and 1995. The treatment centers, located in Pittsburgh, Pennsylvania; Minneapolis,

Behaviors of Adolescents Before and One Year After Treatment

DRUG USE	Before	After
	Percentage	
Weekly Marijuana Use	80.4%	43.8%
Heavy Drinking	33.8	20.3
Hallucinogen Use	31.0	26.8
Stimulant Use	19.1	15.3
SCHOOL PERFORMANCE		
Regular Attendance	62.6	74.0
Grades Average or Better	53.4	79.6
CRIMINAL ACTIVITIES		
Any Illegal Act	75.6	52.8
Any Arrest	50.3	33.9

An evaluation of more than 1,100 adolescents who received substance abuse treatment in residential, short-term inpatient, or drug-free outpatient programs found improvement in rates of drug use and social behavior. Some 53 percent of those treated met or exceeded the minimum recommended stay in treatment.

Minnesota; Chicago, Illinois; and Portland, Oregon, included eight residential programs, nine outpatient drug-free programs, and six short-term inpatient programs.

The 418 adolescents in the residential treatment programs received education, individual and group counseling, and interventions to develop social responsibility. The 292 adolescents in the outpatient drug-free programs received education, skills training, and individual and group counseling. The 467 adolescents in short-term inpatient programs received counseling and a 12-step program. Family therapy was strongly emphasized, and adolescents in these programs were referred to continued outpatient treatment. The average length of treatment for adolescents in the residential, outpatient drug-free, and short-term inpatient programs was 5 months, 1.6 months, and 18 days, respectively.

The adolescents were interviewed when they began treat-

ment and again 1 year after discharge by professional interviewers who were not employed by the treatment centers. Problem severity was determined at the initial interview according to a number of criteria. Dependence on drugs or alcohol was determined from standardized diagnostic measures. To validate self-reports of drug use, one-quarter of the participants were selected randomly to submit urine samples during the posttreatment interview.

Before treatment, 25 percent of the participants used three or more drugs, 36 percent were dependent on alcohol, 64 percent were dependent on marijuana, and 10 percent were dependent on cocaine. In addition to substance abuse problems, 63 percent were diagnosed with a mental disorder and 67 percent were criminally active.

Outcomes Overall

Research has indicated that in general the rate of drug and alcohol use tends to increase during adolescence.

In the present study, however, improvements were observed in many of the areas evaluated, although

some of the participants did not complete their treatment program. Comparing the year before treatment to the year after treatment, the adolescents showed significant declines in the use of marijuana and alcohol, which are considered to be the major drugs of abuse for this age group. Weekly or more frequent marijuana use dropped from 80 percent to 44 percent, and abstinence from any use of other illicit drugs increased from 52 percent to 58 percent. Heavy drinking decreased from 34 percent to 20 percent, and criminal activity decreased from 76 percent to 53 percent. Adolescents also reported fewer thoughts of suicide, lower hostility, and higher self-esteem. In the year following treatment, more adolescents attended school and reported average or better-than-average grades. Some exceptions to the general pattern of improvement were that overall, cocaine and hallucinogen use did not improve during the year after treatment.

Treatment Length and Outcomes

Previous research indicates that a minimum of 90 days of treatment for residential and outpatient drug-free programs and 21 days for short-term inpatient programs is predictive of positive outcomes for adults in treatment. Better treatment outcomes were reported among adolescents who met or exceeded these minimum lengths of treatment than for those who did not. Among the treatment participants, 58 percent of those in residential programs, 27 percent in outpatient drug-free programs, and 64 percent in short-term inpatient programs met or exceeded the minimum stay. In the year following treatment, those who met or exceeded the minimum treatment were 1.52 times more likely to abstain from drug and alcohol use and 1.2 times more likely to not be involved in criminal activity. In addition,

these adolescents were 1.34 times more likely to have average or better-than-average grades.

This study confirms that community-based drug treatment programs designed for adolescents can reduce substance

abuse and have a positive impact on many other aspects of their life, says Dr. Tom Hilton of NIDA's Division of Epidemiology, Services and Prevention Research. These results justify new research to identify the key elements common to effective treatment programs for adolescents, he noted.

Source

- Hser, Y-I.; Grella, C.E.; Hubbard, R.L.; et al. An evaluation of drug treatment for adolescents in four U.S. cities. *Archives of General Psychiatry* 58(7):689-695, 2001. **NN**

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NIDA Clinical Trials Network Begins First Multisite Tests of New Science-Based Drug Abuse Treatments

By Robert Mathias, *NIDA NOTES* Staff Writer

NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) is up and running. Seven research-based drug abuse treatment protocols are being tested under real-world treatment conditions by the network's 6 pioneering regional research centers in collaboration with more than 35 community treatment programs (CTPs). Approximately 3,000 drug abuse patients are expected to participate in this first wave of clinical trials of promising new pharmacological and behavioral drug abuse treatments.

"The CTN is definitely not business as usual," says Dr. Betty Tai, who directs NIDA's CTN Office. In these studies, researchers and practitioners are breaking new ground by working together to see whether and how treatments that are effective under carefully controlled conditions can be adapted and applied effectively with diverse patient populations in a variety of treatment settings, she says. "We expect that protocols that work under these real-world conditions will quickly become the standard of care for physicians, treatment programs, and their patients," she says.

Goals of the Protocols

The CTN's Steering Committee selected the first treatment concepts for testing using three main criteria—solid scientific evidence of efficacy, ease of implementation, and potential to improve public health, Dr. Tai says. Three broad pharmacological and behavioral treatment research concepts were approved from which CTN protocol development teams produced seven treatment protocols for implementation.

Two pharmacological protocols are studying whether buprenorphine/naloxone (BUP/NX) would be more effective in detoxifying opiate-dependent patients than clonidine, a medication that has been used to detoxify opiate addicts. A related protocol is studying the relative effectiveness of different BUP/NX dosing regimens in detoxifying opiate-dependent treatment patients. BUP/NX is a new medication that is nearing FDA approval for treating opiate addiction. Detoxification, the medically supervised withdrawal from an addicting drug on which a patient is physically dependent, represents the first step in treating opiate addiction. Following detoxification, patients are treated with a variety of behavioral and pharmacological approaches in many different treatment settings.



Dr. Betty Tai, Clinical Trials Branch, NIDA; Dr. Robert Forman, University of Pennsylvania, Delaware Valley Node; and Paul Nagy, Duke Addictions Program, North Carolina Node, discuss drug abuse treatment at the CTN meeting in October.

The primary objective of the BUP/NX studies is to evaluate the medication's usefulness in detoxifying opiate addicts in both inpatient and outpatient community treatment settings and to determine the most effective dosing regimens. The lead investigator for these studies, Dr. Walter Ling from the University of California, Los Angeles, directs the CTN's Pacific Region Node. A total of 1,080 patients from 14 CTPs in California, Oregon, New York, Pennsylvania, Connecticut, Virginia, and Maryland are expected to participate in these 3 studies.

"We expect that protocols that work under these conditions will quickly become the standard of care."

Two cognitive treatment protocols are adding motivational enhancement therapy (MET) to standard drug abuse treatment. MET is a brief, nonconfrontational treatment in which a clinician seeks to increase patients' commitment to reducing their drug abuse by heightening their awareness of the harmful personal consequences of that use. In one protocol, a therapist delivers MET in three individual therapy sessions during the first 3 weeks of treatment. In the second protocol, called motivational interviewing, therapists use MET techniques only in



CTN researchers, treatment providers, and NIDA staff met in Los Angeles in October to discuss new treatment protocols and related issues. From left: NIDA Director Dr. Alan I. Leshner; Dr. Ivan Montoya, Clinical Trials Branch, NIDA; Dr. Dennis McCarty, Oregon Health Sciences University, Northwest Node; Kevin McEneaney, Therapeutic Communities of America, Inc.; Allan Bray, Self Help Addiction Rehabilitation, Inc., Great Lakes Node; and Dr. Kathleen Carroll, Yale University, Southern New England Node.

the intake interview given to patients when they enter treatment.

Both MET protocols are trying to determine if patients who are treated with motivational enhancement techniques stay in treatment longer and reduce their drug use more than patients who receive standard treatment alone. The principal investigator for these studies is Dr. Kathleen Carroll of Yale University in New Haven, Connecticut, who directs the CTN's Southern New England Node. It is anticipated that 1,100 patients from 11 CTPs in California, Connecticut, Virginia, Pennsylvania, Oregon, and New York will participate in these 2 studies.

The last two protocols are assessing the benefit of adding a behavioral treatment called motivational incentive (MI) therapy to standard treatment. One protocol is being tested with patients in methadone clinics and the other in drug-free clinics. MI therapy offers patients tangible rewards for remaining drug free. Patients are given the chance to draw for prizes whenever tests indicate they have not used cocaine, amphetamines, methamphetamine, or alcohol. Abstinent patients can win prizes that range from small items such as candy bars and sodas all the way up to larger items, such as clothing, radios, and TVs. Patients have a better chance of winning smaller prizes than larger ones, but the longer they remain abstinent the more chances they get to win.

The primary objective of the MI protocols is to determine if offering tangible incentives for remaining drug free can keep patients in treatment longer and reduce their drug abuse more than standard treatment alone does. Dr. Maxine Stitzer of The Johns Hopkins University School of Medicine in Baltimore, Maryland, and the CTN's Mid-Atlantic Node is the lead investigator for these studies. A total of 800 patients from 5 methadone treatment programs and 6 drug-free clinics in California, Connecticut, Maryland, New York, and Pennsylvania are expected to participate in these 2 studies.

From Protocol to Practice

"We wanted this first wave of protocols to be easy to implement and transfer into community practice," Dr. Tai says. One of the ways the protocols are accomplish-

ing this is by simply adding the therapy being tested to the standard treatment normally used in participating CTPs. Patients in the study are assigned randomly to either the enhanced treatment or standard treatment alone. If a study establishes that patients do better with the enhanced treatment than the standard treatment alone, CTPs can simply use the protocol to add the new treatment to standard treatment as needed, Dr. Tai says.

CTN participants modified research-based treatments to enable them to be sustained in practice, says Dr. Tai. For example, the protocols to implement the MI therapy in the CTPs set the total value of rewards that patients can accumulate for staying drug free considerably lower than the total used in research settings. Researchers initially felt that higher rewards might be needed to provide sufficient incentive for drug abuse patients to remain abstinent. However, practitioners were concerned that such awards would prove too costly for their programs. After much negotiation, the CTN's Steering Committee, which is made up of both researchers and CTP representatives, agreed on a middle ground that kept the maximum value of incentives within a range that CTPs felt they could afford. The bottom line was that CTPs would not have been able to support more costly incentives, no matter how well they worked.

"The CTN has made a very good start towards allowing research and clinical practice to impact one another," says Albert L. Hasson, administrative director of the Matrix Institute on Addiction, an outpatient drug-free clinic in the Los Angeles area that is participating in the CTN.

"The researchers have ideas about how the research should be done based on what has worked in controlled settings. In turn, the CTPs have ideas about how the research should be adapted and integrated into existing treatment settings to best suit the needs of the programs and the patients they serve.

"Participating in a project of this magnitude has been invaluable for us," says Mr. Hasson, who also serves on the CTN's Steering Committee. "To have input into the direction the research will take has enabled our organization to become part of something that could very well shape the future of drug treatment for years to come." **NN**

Gender Differences in Drug Abuse Risks and Treatment

Over the past few years NIDA has made a major research commitment to identifying and understanding differences in the ways that women and men—or girls and boys—are first exposed to drugs, in their risks of abuse and addiction, and in the effectiveness of drug treatment. Understanding these differences, and incorporating that understanding into drug abuse prevention and treatment, can reduce the dangers and improve outcomes. NIDA-supported research has shown that gender differences play a role from the very earliest opportunity to use drugs, that women and men tend to abuse different drugs, that the effects of drugs are different for women and men, and that some approaches to treatment are more successful for women than for men.

Are Women Less Likely Than Men to Abuse Drugs?

Men are more likely than women to have opportunities to use drugs, but men and women given an opportunity to use drugs for the first time are equally likely to do so and to progress from initial use to addiction. However, women and men appear to differ in their vulnerability to some drugs. Both are equally likely to become addicted to or dependent on cocaine, heroin, hallucinogens, tobacco, and inhalants. Women are more likely than men to become addicted to or dependent on sedatives and drugs designed to treat anxiety or sleeplessness, and less likely than men to abuse alcohol and marijuana. There are also differences between men and women who seek treatment for drug abuse. Women in treatment programs are less likely than men to have graduated from high school and to be employed and are more likely than men to have other health problems, to have sought previous drug treatment, to have attempted suicide, and to have suffered sexual abuse or other physical abuse.

Are There Gender Differences In the Biological Effects of Drugs?

Animal research and human studies have revealed that males and females may differ in their biological responses to drugs. In studies of animals given the opportunity to self-administer intravenous doses of cocaine or heroin, females began self-administration sooner than males and administered larger amounts of the drugs. Women may be more sensitive than men to the cardiovascular effects of cocaine. In human studies, women and men given equal doses of cocaine experienced the same cardiovas-

cular response despite the fact that blood concentrations of cocaine did not rise as high in women as in men. In studies involving long-term cocaine users, women and men showed similar impairment in tests of concentration, memory, and academic achievement following sustained abstinence, even though women in the study had substantially greater exposure to cocaine. Women cocaine users also were less likely than men to exhibit abnormalities of blood flow in the brain's frontal lobes. These findings suggest a sex-related mechanism that may protect women from some of the damage cocaine inflicts on the brain.

Does Gender Play a Role in Nicotine Addiction?

Women and men are equally likely to become addicted to nicotine, yet women typically smoke cigarettes with lower nicotine content than those smoked by men, smoke fewer cigarettes per day, and inhale less deeply than men. Overall, however, women are less successful than men in quitting smoking and have higher relapse rates after they do quit. Treatment involving nicotine replacement therapy—nicotine gum or patch—works better for men than for women.

What Are Women's Risks for HIV/AIDS?

Research suggests that there are sex-related differences in some fundamental aspects of the HIV/AIDS disease process. For example, an HIV-infected woman with half the amount of virus circulating in the bloodstream as an infected man will progress to a diagnosis of AIDS in about the same time. And, according to the Centers for Disease Control and Prevention, among cases that progress to a diagnosis of AIDS, drug abuse accounts for a greater percentage of cases among women than among men. Nearly half (47 percent) of all women diagnosed with AIDS are injecting drug users (IDUs), whereas among men, IDUs account for 32 percent of AIDS cases. An additional 19 percent of women, compared with 2 percent of men, with AIDS report having sex with users who inject drugs. In all, drug abuse is nearly twice as likely to be directly or indirectly associated with AIDS in women (66 percent) as in men (34 percent).

For More Information

NIDA's gender-related research is discussed in *Drug Addiction Research and the Health of Women*, available on NIDA's web site: www.drugabuse.gov. **NN**

Treating the Brain In Drug Abuse

By NIDA Director Dr. Alan I. Leshner

Remarkable research and technological advances in the past two decades have proved that brain disruption and damage play central roles in the consequences of drug abuse and addiction. Knowing the nature of a problem, of course, opens the way for systematic attempts to fix it. Thus, today, finding ways to restore normal brain function after it has been changed by drugs is a main goal of NIDA research. (See "NIDA Pursues Many Approaches to Reversing Methamphetamine's Neurotoxic Effects," *NIDA NOTES*, Vol. 15, No. 4). This goal involves two challenges:

- To reverse the brain changes that underlie addiction, and
- To roll back the loss of cognitive and motor functions that occurs when drugs damage and kill brain cells.

To approach the first challenge, NIDA gives top priority to mapping the sequence of neurobiological changes that takes place during the transition from voluntary to compulsive drug taking. Researchers have already identified some of the changes involved in two of the key phenomena associated with addiction: drug tolerance and drug craving. With respect to drug tolerance—the abuser's need for increasing amounts of drug to achieve the desired effect—we now know that drugs significantly increase the availability of dopamine, a neurotransmitter that activates the brain's pleasure circuits. When cells are exposed to repeated surges of dopamine due to chronic drug abuse, they may eventually become less responsive to dopamine signals. In recent months, researchers presented evidence pointing to a specific change in the dopamine receptor molecule that may be instrumental in this loss of responsiveness.

As for drug craving—the intense hunger that drives addicts to seek drugs despite the strong likelihood of adverse consequences—researchers have shown that it is related to widespread alterations in brain activity, but especially to changes in the nucleus accumbens area of the forebrain. An important type of craving experienced by addicts, called cue-induced craving, occurs in the presence of



Finding ways to restore normal brain function after it has been changed by drugs is a main goal of NIDA research.

people, places, or things that they have previously associated with their drug taking. Brain imaging studies have shown that cue-induced craving is accompanied by heightened activity in the forebrain, the anterior cingulate, and the prefrontal cortex—key brain areas for mood and memory. A next step in understanding craving will be to learn what brain processes tie drug abusers' memories so strongly to the desire to take drugs.

Researchers have also made a solid start toward meeting the second challenge posed by drugs' effects on the brain: the restoration of cognitive and motor capabilities lost because of drug abuse. Studies have identified specific brain changes that are likely causes of the persistent losses that are caused by many drugs of abuse. For example, they have shown that:

- Inhalants can produce a variety of deleterious effects—including reduced vision and hearing, impaired movement, and lowered cognitive ability, sometimes to the point of dementia—by stripping the protective myelin sheath from brain fibers;
- Cocaine causes repeated microscopic strokes in the brain, leading to dead spots in the brain's nerve circuitry;
- Methylenedioxymethamphetamine (MDMA) damages serotonin-producing neurons, which play a direct role in regulating aggression, mood, sexual activity, sleep, and sensitivity to pain;
- Methamphetamine amplifies apoptosis—the normal process by which the brain culls defective cells—to the point where it also eliminates healthy cells.

In extreme cases, drugs can cause such severe destruction that users become severely disabled. For example, some methamphetamine abusers have developed a syndrome marked by uncontrollable tremors similar to those seen in Parkinson's disease. The method of heroin self-administration by inhalation known as "chasing the dragon" has rendered some young people nearly comatose with large brain lesions.

To counteract the drug-related brain disruptions that produce addiction and cognitive and motor problems, researchers are seeking to mobilize two important brain capacities. First, under the right circumstances, the brain can self-repair some types of damage. Second, the brain is plastic—that is, when cell losses disrupt the neural circuits that the brain has been using for a specific function, it can learn to use other circuits to perform that function. Plasticity is extremely powerful, as shown by numerous patients’ recoveries from extensive cerebral injuries.

Treatments that alleviate some drug-related brain damage are already here. In fact, in recent months, researchers have demonstrated that methadone therapy ameliorates a particular biochemical abnormality in the brains of opiate abusers. The longer patients stayed in therapy, the more this aspect of their brain biochemistry approached normal. NIDA is currently supporting several similar projects that use new brain imaging techniques to evaluate the full impact of current medication and behavioral treatments on brain neurology and biochemistry. Ultimately, such imaging is likely to become an important tool for assessing patients’ treatment needs, their progress in treatment, and the effectiveness of treatment approaches.

Interventions will be used first to stop ongoing brain damage and repair damaged brain cells, and then to retrain the brain.

Ultimately, researchers envision a two-stage process for helping restore drug abusers’ impaired abilities. Interventions will be used first to stop ongoing brain damage and repair damaged brain cells, and then to retrain the brain. The rationale for this approach is that repairing the brain first will restore lost mental resources and capacities that patients

then can apply in further treatment. Both behavioral and medication treatments may prove to be effective for both stages of treatment. The first stage may benefit from medications already in use to treat neurological conditions that produce brain abnormalities similar to those associated with abuse of some drugs. For example, deprenyl (used in Parkinson’s disease) and acetylcysteine (being tested in Lou Gehrig’s disease) have the potential to help people with drug-related neurological damage.

The new knowledge produced by drug abuse research not only brings present goals closer, it also makes possible new and farther-reaching goals. Today we are applying our understanding of brain processes to the development of treatments that directly target the brain mechanisms of addiction and to the alleviation or reversal of drug-related brain disruption. What we learn in that effort will undoubtedly lead to even more powerful insights and strategies for reducing drug abuse and addiction and their health and social consequences. **NN**

Drug Abuse Treatment Programs Make Gains in Methadone Treatment and HIV Prevention

By Steven Stocker, *NIDA NOTES* Contributing Writer

Drug abuse treatment programs have substantially improved their methadone treatment practices and increased their HIV prevention efforts since the late 1980s, according to recent NIDA-funded research. These improvements appear to be partly the result of NIDA's efforts to improve drug abuse treatment and HIV/AIDS outreach.

Clinical studies conducted in the late 1980s and early 1990s indicated that methadone treatment is more likely to reduce heroin use if the dose level is at least 60 milligrams per day (mg/day), if patients are given a voice in determining their dose levels, and if no restriction is placed on treatment duration. Subsequent research, however, indicated that the majority of the Nation's methadone treatment facilities were dispensing methadone doses less than 60 mg/day, were not giving patients a voice in dosage decisions, and were encouraging patients to stop taking methadone in 6 months or less.

In response to this situation, NIDA and other Federal agencies took steps to improve methadone treatment. NIDA funded an Institute of Medicine report that recommended changes in heroin addiction treatment practices and their regulation. NIDA also funded the development of a quality assurance program that evaluates methadone treatment facilities in terms of patient outcomes. In addition, the Center for Substance Abuse Treatment (CSAT) developed a set of methadone treatment guidelines and distributed them to State substance abuse agencies and treatment providers around the country.

To determine whether these efforts were in fact improving methadone treatment practices, in 1995 Dr. Thomas D'Aunno of the University of Chicago and his colleagues at the University of Michigan in Ann Arbor collected data from 116 methadone treatment facilities located throughout the country and compared them with data collected on these same facilities in 1988 and 1990. Results showed improvement during the 7-year period, particularly regarding methadone dosage. The average dose was

45 mg/day in 1988 and 46 mg/day in 1990. By 1995, however, the average dose had increased to 59 mg/day. Also, more programs were allowing patients to participate in dosage decisions, and more programs were waiting at least a year before encouraging patients to stop taking methadone.

The treatment facilities most likely to conduct HIV prevention activities were those that had more patients at high risk of HIV infection, more resources, and lower patient-to-staff ratios.

"Although these results show that methadone treatment facilities have made substantial improvements, we still need to make more progress," says Dr. D'Aunno. "We found an average dose of 59 mg/day in our sample of treatment facilities, but recent research indicates that doses between 80 and 100 mg/day may be the most effective in reducing heroin use." (See "High-Dose Methadone

Improves Treatment Outcomes," *NIDA NOTES*, Vol. 14, No. 5).

The study found differences in treatment practices in different areas of the country and for different population groups. Dr. D'Aunno suggests that efforts targeted at particular groups of programs may be a further step to improve treatment.

Dr. Bennett Fletcher of NIDA's Division of Epidemiology, Services, and Prevention Research agrees that efforts to improve methadone treatment practices should continue but adds that misunderstandings some patients have about methadone may also contribute to the problem. For example, he says, some patients attribute adverse effects to methadone that it actually does not cause. "These patients may develop medical or dental problems while taking heroin, but they don't notice them either because of heroin's analgesic effect or because they are distracted by withdrawal symptoms during abstinence," he says. "Once they're in methadone treatment and physiologically stabilized, the medical or dental problems are unmasked. It is easy to blame methadone for these problems, when in fact they were pre-existing." These misunderstandings may cause some patients to request lower methadone doses or to stop methadone prematurely, says Dr. Fletcher.

The Bandwagon Effect

Dr. D'Aunno, along with colleagues at the University of Iowa in Iowa City and the Centers for Disease Control and Prevention in Atlanta, also evaluated treatment facilities' HIV prevention efforts, including HIV testing, counseling, and outreach. For this project, they used data collected from the sample of methadone treatment facilities plus other substance abuse treatment facilities for a total of 618 facilities.

As with the methadone treatment practices, the investigators found that the facilities had made substantial improvements in their HIV prevention efforts over the period from 1988 to 1995. In both 1988 and 1990, only 39 percent of the facilities provided HIV testing and counseling, but by 1995, 61 percent were providing these services. Also, 51 percent of the facilities in 1988 and 65 percent in 1990 were engaging in HIV outreach, but by 1995 this had increased to 75 percent.

The investigators found that the treatment facilities most likely to conduct HIV prevention activities were those that had more patients at high risk of HIV infection, more resources, and lower patient-to-staff ratios. Also, these facilities generally were publicly rather than privately funded and had clinical supervisors who supported HIV prevention practices.

Perhaps the most important factor in promoting HIV prevention practices, however, seemed to be pressure

from people in the drug abuse treatment field. "When the HIV epidemic first started, many treatment facilities were uncertain how to react," says Dr. D'Aunno. "As some facilities began conducting HIV testing, counseling, and outreach, pressure began to mount for other facilities to do the same. This eventually created a bandwagon effect."

NIDA helped get the bandwagon going by supporting research programs in which scientists worked together with practitioners to develop effective HIV/AIDS outreach techniques, according to Dr. D'Aunno. "These programs set a good example for treatment providers," he says. "The providers saw local researchers and other providers working together on HIV prevention, and they decided to follow their lead."

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Adding More Counseling Sessions and 12-Step Programs Can Boost Drug Abuse Treatment Effectiveness

By Robert Mathias, NIDA NOTES Staff Writer

Drug abuse treatment programs can significantly increase the likelihood that patients will stay in treatment and remain abstinent by offering them more group and individual counseling opportunities and encouraging them to participate in complementary 12-step programs, such as Narcotics Anonymous, according to NIDA-supported research.

A series of studies by Dr. Robert Fiorentine of the University of California, Los Angeles (UCLA) and his colleagues from the UCLA Drug Abuse Research Center has been looking at how individual treatment components affect patient outcomes. One study found that patients who attended more group and individual counseling sessions had significantly lower levels of drug use during and after treatment than those who participated less frequently. Even among patients who completed the treatment program, those who participated more frequently in counseling had lower rates of relapse than those who participated less.

Increasing Counseling Opportunities

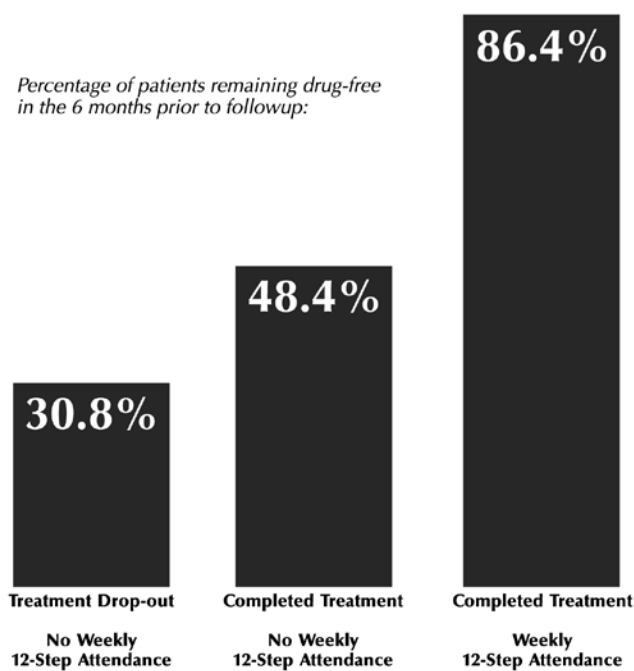
Dr. Fiorentine then examined whether treatment programs could improve their effectiveness by providing more opportunities for patients to participate in counseling. This study assessed the treatment outcomes of 330 patients in 26 Los Angeles outpatient programs. Seventeen programs had added treatment services and increased counseling opportunities by hiring additional counselors.

Even minimal increases in counseling opportunities may produce impressive gains in treatment outcomes.

This study found that patients in the enhanced programs attended about four more group counseling sessions and one more individual counseling session each month than did patients in comparison programs. Patients in enhanced programs also used drugs 40 percent less than did patients in comparison programs in the 6 months following an initial in-treatment assessment; in the last month, they used drugs 60 percent less. When the researchers examined whether patient characteristics or

Participation in Drug Abuse Treatment and 12-Step Program Improves Treatment Outcomes

Percentage of patients remaining drug-free in the 6 months prior to followup:



other treatment services provided by enhanced programs may have affected these results, they found that the frequency of patients' participation in individual and group counseling accounted for virtually all of the differences in post-treatment drug use.

This study suggests that even minimal increases in counseling opportunities may produce impressive gains in treatment outcomes, the researchers note. By hiring only one or two additional counselors, enhanced programs could reduce their counselors' caseloads and offer more group and individual counseling sessions, Dr. Fiorentine says. "It was only a few more sessions per week but, since patient attendance in these sessions often depends on session availability, it made a difference," he says.

Adding 12-Step Programs

Because many patients in Los Angeles area treatment programs attend 12-step programs either on their own or as part of their treatment regimen, Dr. Fiorentine and his colleagues also examined the relationship between

participation in such programs and the effectiveness of drug abuse treatment. One study found that patients who attended at least one 12-step meeting per week after completing drug abuse treatment had much lower levels of drug use than those who participated less frequently or not at all. In this study, the researchers interviewed 262 patients in 26 Los Angeles area drug abuse treatment programs during treatment and 6 and 24 months later. Almost half of these patients had attended a 12-step meeting in the 6 months preceding the last interview.

During this 6-month period, only about 22 percent of weekly 12-step participants had used an illicit drug. By contrast, 44 percent of those who attended 12-step programs less than once a week or not at all during that period had used an illicit drug. Additional analyses indicated that the more favorable outcomes of frequent 12-step participants could not be attributed to differences in motivation or to other posttreatment activities, such as attending other aftercare programs. Weekly 12-step participants did score slightly higher than nonparticipants on a scale of self-reported measures of recovery motivation. However, statistical analyses indicated the differences in motivation accounted for little if any of the more favorable outcomes for frequent 12-step participants. The important difference between the two groups was not recovery motivation but at least weekly 12-step participation, the researchers say.

This study's findings suggest that 12-step programs can serve as a useful and inexpensive aftercare resource that can help many patients to maintain abstinence from drugs and alcohol after they complete drug abuse treatment, say the researchers.

Findings from another study by Dr. Fiorentine indicate that participation in 12-step programs before and during drug abuse treatment also may benefit patients' treatment engagement and recovery. In this study, more than two-thirds of 419 patients who entered outpatient treatment programs in Los Angeles during a 2-month period were attending 12-step meetings in the 3 months before they entered treatment. About 45 percent were attending meetings at least once a week.

Patients who attended 12-step meetings regularly before entering drug abuse treatment stayed in treatment longer and were more likely to complete the treatment program and participate in posttreatment 12-step programs, the study found. Moreover, an assessment conducted 8 months after the initial intake interview showed that patients who attended 12-step meetings at least once a week while they were participating in conventional drug abuse treatment had significantly higher rates of abstinence than patients who participated in only one or the other of those programs.

These findings suggest an "additive effect" on the recovery process from concurrent participation in drug abuse treatment and 12-step programs, Dr. Fiorentine says. "You get a better outcome with both than if you do either alone," he concludes.

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The State of the Art in Drug Addiction Treatment

By NIDA Director Dr. Alan I. Leshner

NIDA's recent publication, *Principles of Drug Addiction Treatment: A Research-based Guide*, distills the lessons of 25 years of scientific investigation. *Principles* is written for health care providers, to stimulate their awareness of the variety of effective approaches to drug treatment. It is also for patients and potential patients and their families, to help them understand the nature of addiction and to tell them about scientifically based treatments and what to expect if they enter treatment. And it serves planners and policymakers as well, enabling them to make informed decisions concerning treatment programs.

In short, this book is for you. That is why NIDA mailed a copy in October to every *NIDA NOTES* reader in the United States. If you have not yet read yours, I urge you to do so. If you did not receive a copy or want additional copies to pass on to friends or colleagues, you can obtain copies from the National Institute on Drug Abuse's DRUG PUBLS Research Dissemination Center, Educational Materials Online Catalog's Web site drugpubs.drugabuse.gov.

Based on a yearlong review of treatment research, *Principles* describes where we stand today in our quest for the most effective, replicable treatments for drug abuse. The book contains many important messages, but one is central.

Treatment is effective. Scientifically based drug addiction treatments typically reduce drug abuse by 40 percent to 60 percent. These rates are not ideal, of course, but they are comparable to compliance rates seen with treatments for other chronic diseases such as asthma, hypertension, and diabetes. Moreover, treatment markedly reduces undesirable consequences of drug abuse and addiction—such as unemployment, criminal activity, and HIV/AIDS and other infectious diseases—whether or not patients achieve complete abstinence. Research has shown that every \$1 invested in treatment saves \$4 to \$7 in costs related to drug abuse.



That treatment is effective will not be news to treatment providers or to the tens of thousands of individuals and families who have benefited from treatment. Unfortunately, many members of the public still mistakenly doubt that treatment can help someone overcome addiction, perhaps because, as *Principles* explains, recovery from addiction can be a long-term process and frequently requires multiple episodes of treatment. To these people, the message of *Principles* is: We have the tools, let's do the job.

Based on a year-long review of treatment research, Principles describes where we stand today in our quest for the most effective, replicable treatments for drug abuse.

By describing the current state of the art, *Principles* also clarifies the many challenging research pathways that remain to be traversed on the way to our goal of fully effective treatment for every patient. To cite just a few of the more pressing objectives, we need to:

- Understand the complete behavioral and biological mechanisms of addiction;
- Obtain a full picture of the transition from drug use to drug addiction and the stages of recovery in order to fashion optimal treatments for patients at every point along that trajectory;
- Understand better how gender affects vulnerability to drug addiction and the response to treatment in order to more appropriately tailor treatments for men and women;
- Develop additional medications for treating opiate addiction and effective medications for addiction to stimulants such as cocaine and methamphetamine;
- Continue to test the effectiveness of treatments in real-life community-based settings.

NIDA is adjusting its organizational structure and has instituted key procedures to expedite the next stage of our treatment research journey. As I write, the Institute is completing the creation of a new Division of Treatment Research and Development (DTRD). The new Division

will facilitate research on combined medication and behavioral treatments, which appears to be an essential strategy for improving many patients' chances of successful treatment outcomes.

With the support of its Medications Development Division, one of DTRD's predecessors, NIDA has developed cooperative links with the pharmaceutical industry that enable NIDA-supported researchers to obtain proprietary chemical compounds for testing as possible medications for drug abuse. As a first fruit of these partnerships, a new cocaine "vaccine" is currently being tested in a large-scale clinical trial. Based on NIDA-supported basic studies, this new medication appears to reduce the desire to use cocaine by blocking the drug's euphoric effects. NIDA also is exploring ways for new medications to reach more of those in need. The demonstrated effectiveness of buprenorphine and naloxone in treating opiate addiction, for example, suggests that these drugs may be safely dispensed by physicians in controlled settings.

With respect to behavioral therapies, NIDA has established a three-stage process for developing, evaluating, and introducing new approaches into mainstream clinical use. The potential of each proposed new behavioral treatment is first explored in a small pilot study. If the preliminary data are promising, the treatment is tested in a full-scale clinical trial. If the trial demonstrates efficacy, clinicians take the treatment out of the research setting and adapt it

as necessary for mainstream use. This new model establishes the first clear benchmarks for testing, comparing, and implementing behavioral treatments. To date, two new treatments have passed the preliminary stage of testing and moved on to the clinical trials stage.

As regular readers of *NIDA NOTES* are aware, the largest initiative in NIDA's history is focused on treatment. This is the National Drug Abuse Treatment Clinical Trials Network (CTN), in which research centers ally with nearby community treatment programs to set research goals and participate in large-scale multisite clinical trials. NIDA recently announced the establishment of the first five CTN locations. Ultimately, the CTN will provide a nationwide coordinating infrastructure with sufficient patient numbers and diversity to enable scientists to optimize treatment effectiveness by matching treatments with appropriate patient groups.

There is a pattern in scientific research in which knowledge and techniques are slowly, painstakingly developed until they reach a critical mass that makes possible a more rapid and direct approach to problem solving. This first edition of *Principles* reflects the power of this pattern of progress to produce epochal advances in public health and welfare. With well-defined questions and powerful new technologies and research techniques coming on line every year, we do not expect to wait very long before publishing the second edition of *Principles*. **NN**

Thirteen Principles of Effective Drug Addiction Treatment

More than two decades of scientific research have yielded a set of fundamental principles that characterize effective drug abuse treatment. These 13 principles, which are detailed in NIDA's new research-based guide, *Principles of Drug Addiction Treatment: A Research-based Guide*, are:

1. **No single treatment is appropriate for all individuals.** Matching treatment settings, interventions, and services to each patient's problems and needs is critical.
2. **Treatment needs to be readily available.** Treatment applicants can be lost if treatment is not immediately available or readily accessible.
3. **Effective treatment attends to multiple needs** of the individual, not just his or her drug use. Treatment must address the individual's drug use and associated medical, psychological, social, vocational, and legal problems.
4. **Treatment needs to be flexible** and to provide ongoing assessments of patient needs, which may change during the course of treatment.
5. **Remaining in treatment for an adequate period of time is critical for treatment effectiveness.** The time depends on an individual's needs. For most patients, the threshold of significant improvement is reached at about 3 months in treatment. Additional treatment can produce further progress. Programs should include strategies to prevent patients from leaving treatment prematurely.
6. **Individual and/or group counseling and other behavioral therapies are critical components of effective treatment for addiction.** In therapy, patients address motivation, build skills to resist drug use, replace drug-using activities with constructive and rewarding nondrug-using activities, and improve problem-solving abilities. Behavioral therapy also facilitates interpersonal relationships.
7. **Medications are an important element of treatment for many patients,** especially when combined with counseling and other behavioral therapies. Methadone and levo-alpha-acetylmethadol (LAAM) help persons addicted to opiates stabilize their lives and reduce their drug use. Naltrexone is effective for some opiate addicts and some patients with co-occurring alcohol dependence. Nicotine patches or gum, or an oral medication, such as bupropion, can help persons addicted to nicotine.
8. **Addicted or drug-abusing individuals with coexisting mental disorders should have both disorders treated in an integrated way.** Because these disorders often occur in the same individual, patients presenting for one condition should be assessed and treated for the other.
9. **Medical detoxification is only the first stage of addiction treatment** and by itself does little to change long-term drug use. Medical detoxification manages the acute physical symptoms of withdrawal. For some individuals it is a precursor to effective drug addiction treatment.
10. **Treatment does not need to be voluntary to be effective.** Sanctions or enticements in the family, employment setting, or criminal justice system can significantly increase treatment entry, retention, and success.
11. **Possible drug use during treatment must be monitored continuously.** Monitoring a patient's drug and alcohol use during treatment, such as through urinalysis, can help the patient withstand urges to use drugs. Such monitoring also can provide early evidence of drug use so that treatment can be adjusted.
12. **Treatment programs should provide assessment for HIV/AIDS, hepatitis B and C, tuberculosis and other infectious diseases,** and counseling to help patients modify or change behaviors that place them or others at risk of infection. Counseling can help patients avoid high-risk behavior and help people who are already infected manage their illness.
13. **Recovery from drug addiction can be a long-term process** and frequently requires multiple episodes of treatment. As with other chronic illnesses, relapses to drug use can occur during or after successful treatment episodes. Participation in self-help support programs during and following treatment often helps maintain abstinence.

Principles of Drug Addiction Treatment: A Research-based Guide can be obtained by visiting the NIDA DRUG PUBLS Research Dissemination Center's Web site at drugpubs.drugabuse.gov. **NN**

Medications Reduce Incidence of Substance Abuse Among ADHD Patients

By Steven Stocker, *NIDA NOTES* Contributing Writer

Attention-deficit hyperactivity disorder (ADHD) causes difficulties in paying attention, keeping still, and suppressing impulsive behaviors. It can lead to problems in school and on the job and create tensions with family members and other people. In addition, research has shown that children with ADHD have an elevated risk of becoming abusers of drugs and alcohol. Studies that have tracked children to adulthood have found higher rates of transition to abuse among those with ADHD compared to those without the disorder. Conversely, studies with adult substance abusers, particularly cocaine abusers, have found that when they were children a high percentage had ADHD that was undiagnosed and therefore untreated.

NIDA-supported researchers have been trying to learn why ADHD increases the risk of drug and alcohol abuse. Two possible explanations have been suggested. First, the disorder itself may be responsible. Alternatively, the medications used to treat the disorder may be to blame.

ADHD is usually treated with behavioral therapy and prescription stimulants, especially Ritalin® (methylphenidate), Dexedrine®, or Adderall®. Such therapy frequently reduces symptoms, but some clinicians have feared that giving prescription stimulants to children may get them in the habit of taking stimulants, and, as a result, they may be more likely to take illicit stimulants, such as cocaine and methamphetamine. Another possibility is that the use of prescription stimulants for treating ADHD may sensitize the brain to the rewarding properties of stimulants, and, as a result, patients who use illicit stimulants may be more likely to become addicted to them.

Some children treated for ADHD with stimulant medications experience adverse effects, such as tics or loss of appetite. These children may be treated instead with tricyclic antidepressants (TCAs), a class of medications that includes imipramine, desipramine, and nortriptyline. Just as with mild stimulants, some clinicians are concerned that giving these mood-altering medications to children may get them in the habit of taking drugs to feel better and so they may be more at risk of using illicit drugs.

If ADHD treatment medications increase the risk of drug abuse, then using them might do more harm than good over the course of the child's lifetime. However, two new NIDA-supported studies suggest that treatment medications may be part of the solution to drug abuse in ADHD, rather than the problem.

One study found that children who were medicated for their ADHD were less likely to become substance abusers during 4 years of followup than were children with ADHD who were not medicated. The other study found that administering an ADHD medication to adult cocaine abusers with the disorder reduced their cocaine use.

Boys Treated for ADHD Abuse Drugs Less Than Untreated Boys

Researchers at Massachusetts General Hospital and the Harvard Medical School, both in Boston, compared the incidence of substance abuse and dependence in 56 boys with ADHD who were being treated with either stimulants or TCAs at the beginning of the study, 19 boys with ADHD who were not receiving any medications, and 137 boys without ADHD. All boys were Caucasian and were



Children with ADHD often have trouble concentrating and keeping still, which can lead to problems in school.

followed for 4 years and then evaluated for abuse of or dependence on marijuana, alcohol, hallucinogens, stimulants, or cocaine. At the time of evaluation, the boys were at least 15 years old.

Treating ADHD with medications appeared to reduce the tendency to abuse drugs and alcohol. While 75 percent of the unmedicated ADHD boys had started abusing these substances in the previous 4 years, this was true of only 25 percent of the medicated ADHD boys and 18 percent of the boys without ADHD. The researchers calculated that treating ADHD with medications reduced the risk of substance abuse or dependence by 84 percent.

Dr. Joseph Biederman, the principal investigator of the study, calls this very important information for the field of pediatrics. "These are the first data to refute the argument that ADHD medications increase the risk that children will become addicts," he says. "There have been studies consistent with these findings for many years, but now we have solid statistical evidence that these medications decrease, rather than increase, vulnerability to addiction, at least in adolescent Caucasian boys."

Why treatment with medications should reduce the incidence of substance use disorders in boys with ADHD is not known, says Dr. Biederman, just as what causes ADHD and how medications reduce ADHD symptoms are also unknown. "I can only speculate that by reducing ADHD symptoms, the medications allow the children to interact better with their families and friends and to perform better in school," he says. "As a result, they are less likely to be ridiculed and rejected by other children and to fail in school. Because of this, they are less likely to be depressed and to take drugs in an attempt to treat their depression." He says that another reason may be that the medications reduce the tendency of ADHD children to be impulsive, which often leads them to engage in risky activities, such as taking drugs.

Other researchers have reported that some adult cocaine abusers with childhood histories of ADHD state that when they first started using cocaine, the drug initially improved their ADHD symptoms. Their concentration improved, they were less impulsive, and they felt calmer. This would suggest that young people with ADHD who abuse cocaine and other stimulants may be doing so to self-medicate their ADHD symptoms rather than to treat depression resulting from rejection and failure.

"In some cases, young people with ADHD are not properly diagnosed and treated, and, as a result, they have terrible problems," says Dr. Arthur Horton of NIDA's Division of Treatment Research and Development (DTRD). "Their lives are not going well, so they try different things to make themselves feel better. They don't

know that Ritalin® will alleviate their symptoms. If they happen to try cocaine, they might find that it initially makes them more focused and able to deal with life, so they keep taking it, and that's how they get hooked."

DTRD Director Dr. Frank Vocci points out that more research needs to be done before definite conclusions can be drawn about the relationship between ADHD therapy and substance abuse. "As it stands, this study clearly supports the idea that medications protect individuals with ADHD from becoming substance abusers during childhood and adolescence," he says. "However, whether or not they become substance abusers when they reach adulthood is still an open question."

Dr. Biederman says that his group is continuing to collect data on his sample as they age. Another followup study is currently under way on the young men, who are now between 16 and 27 years old. This study should help answer the question of whether ADHD medication therapy can protect against substance abuse in late adolescence and early adulthood. The researchers are also following a group of girls with ADHD and a comparison group of girls without ADHD. A key question to be answered will be whether gender differences exist in the effects of stimulants, including the effects on substance abuse.

Treatment That Includes Methylphenidate Helps Adult Cocaine Abusers With ADHD

In addition to helping protect children with ADHD from becoming substance abusers, methylphenidate may also help adult cocaine abusers with ADHD reduce their drug use. In a pilot study, Dr. Frances Levin and researchers at Columbia University in New York City gave methylphenidate for up to 12 weeks to 12 adult cocaine abusers with ADHD. Patients also received individual weekly relapse prevention therapy, which involved identifying situations in which they were likely to return to cocaine use and developing strategies to avoid cocaine use in these situations. Of the 12 patients who entered the study, 7 could be reached for a 3-month assessment. Patients reported a reduction in ADHD symptoms, cocaine use, and craving; urine tests confirmed that their cocaine use had in fact decreased significantly.

At present, Dr. Levin cannot say whether methylphenidate, the behavioral therapy, or a combination of both was responsible for the positive results. To answer this question and to determine whether these preliminary results can be reproduced among other cocaine abusers with ADHD, she is conducting a large clinical trial in which neither the patients nor their therapists know whether the patients are receiving methylphenidate or placebo.

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Drug Abuse and Mental Disorders: Comorbidity Is Reality

By NIDA Director Dr. Alan I. Leshner

A quarter century of basic and clinical research has provided us with a substantial number of scientifically developed and tested pharmacological and behavioral techniques for treating drug abuse and addiction. A main thrust of NIDA's current research is to discover which combinations of treatments and services work best for individual patients with particular constellations of problems. The goal is to customize treatment for every patient, including those with coexisting problems such as multiple drug abuse, drug abuse-related infectious diseases, histories of sexual abuse, or homelessness.

Drug abusers who have concurrent, or comorbid, mental health problems are at the top of the list of those who will benefit from this research, for two reasons. First, they are numerous. Recent epidemiologic studies have shown that between 30 percent and 60 percent of drug abusers have concurrent mental health diagnoses including personality disorders, major depression, schizophrenia, and bipolar disorder. Second, drug abusers with mental illness comorbidity are more likely to engage in behaviors that increase risk for HIV/AIDS. For example, two studies of injecting drug abusers have found that antisocial personality disorder (APD) is associated with a higher frequency of needle sharing.

In order to direct treatment and services research to where it is most needed, NIDA supports epidemiologic studies of mental health comorbidities. The results to date suggest that the most common are personality disorders including APD and borderline personality disorder; anxiety disorders including post-traumatic stress disorder (PTSD); and depression. Some evidence suggests that men who use drugs are more likely to have APD, while women and minorities are more likely to have depression or PTSD. While people with schizophrenia do not constitute a large portion of the drug-abusing population, an extraordinarily high percentage of people with this disease abuse drugs.



Recent epidemiologic studies have shown that between 30 percent and 60 percent of drug abusers have concurrent mental health diagnoses including personality disorders, major depression, schizophrenia, and bipolar disorder.

A concurrent mental disorder can complicate drug abuse treatment in a multitude of ways. For example, research suggests that clinically depressed individuals have an exceptionally hard time resisting environmental cues to relapse—that is, urges to resume drug taking that commonly occur when abstinent addicts encounter people, places, or things associated with their previous drug use. In some cases, treatment for mental disorders must be adjusted because of concurrent drug abuse. For example, opiate users with

anxiety disorders are considered poor candidates for standard therapy with anti-anxiety drugs of the benzodiazepine class because these drugs can cause a second addiction.

NIDA-supported researchers have identified effective ways to tailor treatment for some patients with dual diagnoses. In one study, opiate addicts with APD responded better when standard contingency man-

agement therapy was modified. In the standard type of this therapy, patients receive small rewards for abstinence that become progressively greater the longer abstinence is maintained. In the modified version, treatment professionals gave more frequent rewards for desirable behaviors, such as attending scheduled counseling sessions and testing clean for drugs. (See "Specialized Approach Shows Promise for Treating Antisocial Drug Abuse Patients," *NIDA NOTES*, Vol. 11 No. 4). In another study, drug craving was reduced among teenage cocaine abusers with bipolar disorder who receive lithium, and in depressed heroin abusers who were treated with imipramine. (See "Treating Mood Disorders in Drug Abuse Patients," *NIDA NOTES*, Vol. 13 No. 6). In this issue of *NIDA NOTES*, we report on promising results with methylphenidate and antidepressants in children with attention-deficit/hyperactivity disorder (ADHD) and with

methylphenidate in adult cocaine abusers with ADHD. (See “Medications Reduce Incidence of Substance Abuse Among ADHD Patients,” *NIDA NOTES*, Vol. 14, No. 4).

Just as the co-occurrence of drug abuse and mental health problems presents special problems for treatment, so does it also for research. The problems arise in part because drug abuse and other mental health disorders can intertwine in several ways. For example, successful treatment of cocaine addiction often also dispels concurrent depression, while nicotine addicts’ depression commonly persists after successful smoking cessation treatment. Such variations make it difficult to generalize treatment research findings across large patient groups.

As a result, progress has been made in relatively small increments. Another problem facing researchers is that a study population that is ostensibly uniform because all individuals have the same drug abuse and mental health disorders may actually be nonuniform. The reason is that the relationship between the two disorders may vary in different patients. For example, some people with a mental disorder may initiate drug use as an inappropriate form of self-medication, some people who take drugs may develop mental disorders as a consequence of their drug use, and a third group may simply have the two disorders at the same time. If an intervention is evaluated in a study population where some patients have drug abuse as a primary disorder and others as a secondary disorder, the treatment may appear to be ineffective even though it works well for one of these subgroups.

A structural difficulty that complicates research on drug abuse and mental illness comorbidity is that few drug abuse treatment programs treat enough patients with a

particular mental health disorder to easily generate the preliminary data necessary to justify a full-scale study of

a treatment for the disorder. To overcome this difficulty and accelerate the pace of discovery, NIDA’s Behavioral Therapy Development Program places special emphasis on pilot studies in drug abuse and mental illness comorbidity. The program represents a kind of research “venture capital,” making possible the rapid initial testing of many ideas, the best of which will then proceed rapidly to further, more defini-

tive testing. Starting next year, NIDA’s Clinical Trials Network will accelerate this wider testing by facilitating the recruitment of large numbers of patients with the drug abuse and comorbidity characteristics that treatments are designed to address. (See “Clinical Trials Network Will Speed Testing and Delivery of New Drug Abuse Therapies,” V14-1, April 1999.)

Drug abuse and mental health professionals both confront the difficulty of providing effective care to patients whose problems overlap two health care specialties that share much, but are also in many ways very distinct. In response to this situation, NIDA and the National Institute of Mental Health have been actively collaborating on epidemiologic and treatment research on comorbidity. For example, the two Institutes are examining the problem of treating the relatively small population of patients who abuse drugs and also have severe mental disorders, such as schizophrenia or bipolar disorder. These patients require integrated specialty treatments.

In drug abuse as in other areas of health care, isolated disorders are simplest to study and treat, but comorbidity is reality for many individuals. NIDA research has laid the foundation for successful investigations of these complex realities. **NN**

Drug abusers who have concurrent, or comorbid, mental health problems are at the top of the list of those who will benefit from this research.

Clinical Trials Network Will Speed Testing and Delivery Of New Drug Abuse Therapies

By Patrick Zickler, *NIDA NOTES* Staff Writer

Over the past quarter century, NIDA research programs have produced dramatic advances in understanding drug abuse and addiction and led to the development of an array of new treatments and therapies to help patients with drug abuse problems. But, in order to fulfill their promise, the advances achieved in drug abuse research centers must reach patients in the community-based settings where most treatment is provided. To enhance the delivery of scientifically based treatments to drug abuse patients, NIDA is establishing the National Drug Abuse Treatment Clinical Trials Network.

The Clinical Trials Network (CTN) will provide a structured partnership in which NIDA, treatment researchers, and community-based service providers will cooperatively develop, validate, refine, and deliver new treatment options to patients in community-level clinical practice.

"The Clinical Trials Network is a revolutionary advance in the study and treatment of drug abuse and addiction. It is the most important initiative the Institute has ever undertaken," says NIDA Director Dr. Alan I. Leshner.

The CTN framework will consist of Regional Research and Training Centers (RRTCs) linked in partnership with 5 to 10 or more community-based treatment programs (CTPs). These RRTC/CTP partnerships will constitute CTN Research Nodes. "Each Node will include CTPs that represent a variety of patient populations and will be linked through the Network with other Nodes throughout the country," says Dr. Stephen Zukin, director of NIDA's Division of Clinical and Services Research. "This means the Clinical Trials Network will provide a broad and powerful infrastructure for rapid multisite testing of promising science-based therapies. Patients in community-based treatment settings across the country will benefit, and benefit sooner, from well-developed science-based care."

The CTN will be national in scope but anchored on community-level programs. The size and diversity of patient populations participating in CTN studies will provide a resource for concurrent testing of promising therapies and will make it possible to conduct comprehensive investigations of factors such as environmental and genetic deter-

minants of vulnerability to drug dependence and abuse. CTN investigators and treatment providers and others in the broader research community will have access to the research database generated by the CTN.

The CTN will help meet one of the principal needs identified in *Bridging the Gap Between Research and Practice*, the Institute of Medicine's 1998 report on community-based drug and alcohol treatment. The report recommended the development of an infrastructure to facilitate research within a network of community-based treatment programs. NIDA announced its intention to establish the CTN in December 1998, and has issued a Request for Applications soliciting cooperative agreement applications from established clinical investigators to participate in the Clinical Trials Network.

NIDA has committed first-year funding of \$10 million for the CTN. The Institute plans to make as many as four awards, for project periods up to 5 years, during the first year. When fully developed, the Network will include from 15 to 30 Nodes incorporating well over 100 community treatment facilities.

The CTN partnership is designed to meet a range of objectives that include:

- supporting studies of behavioral, pharmacological, and combined behavioral and pharmacological treatment interventions of proven efficacy in rigorous, multisite clinical trials to determine effectiveness across a broad range of treatment settings and patient populations;
- furthering the development of effective treatments by integrating behavioral, pharmacological, and treatment research;
- investigating the impact of advances in treatment research on community-level treatment practices;
- ensuring that treatment research in drug abuse and addiction meets the needs of the wider community, including minorities, women, children, and underserved populations;

-
- fostering the collaboration of community treatment practitioners and researchers to provide opportunities for exchange of ideas, information, and values between the treatment and academic communities; and
 - determining the impact of the transport of novel, effective treatments in the community on the incidence and prevalence of various other illnesses and conditions, including HIV and hepatitis.

For More Information

Additional information about the Clinical Trials Network can be found at www.nida.nih.gov/funding/clintrials.html.



Antistress Medications May Help Drug Abuse Patients Avoid Relapse

A class of medications currently being developed by several pharmaceutical companies may help drug abuse patients avoid relapse after experiencing stress. Called CRF antagonists, the compounds block the action of corticotropin-releasing factor (CRF), a naturally occurring chemical in the brain. Scientists think that CRF may play a key role in producing arousal, anxiety, and other emotional responses to stress.

Dr. Yavin Shaham, formerly of the University of Toronto and now in NIDA's Intramural Research Program in Baltimore; NIDA grantee Dr. Jane Stewart of Concordia University in Montreal; and their colleagues at Concordia University and the Addiction Research Foundation in Toronto have conducted a series of studies to determine whether CRF antagonists can prevent stress-induced relapse to drug-seeking in rats. In these studies, rats were trained to press a lever to receive a dose of cocaine or heroin. After the rats learned this behavior, the supply of drugs was terminated so that pressing the lever no longer resulted in a dose of drug. As a result, the rats reduced their lever pressing to practically nothing. However, when the rats were given mild intermittent footshocks for 10 to 15 minutes, they started to press the lever again as soon as it became available, even though they did not receive any drug. This indicates that stress can reinstate drug seeking in rats, just as it is reported to do in human addicts, says Dr. Stewart.

The researchers found that giving the rats a CRF antagonist prior to giving them footshocks could greatly reduce the rate at which the rats would press the lever again. However, the compound had no effect when the rats were pressing a lever to receive a drop of sugar solution that they could drink. "This suggests that the CRF antagonist blocks stress-induced relapse to drug seeking specifically and does not produce its effects by interfering with the animal's ability to press the lever," says Dr. Stewart.

Results such as these have interested staff in NIDA's Medications Development Division (MDD) in the potential of CRF antagonists for treating drug abuse relapse. "What's so interesting about CRF antagonists is that evidence suggests that they may be useful in treating relapse to a variety of drugs, including cocaine, heroin, and nicotine," says Dr. Jane Acri of MDD. "This is particularly important considering that people who abuse drugs often abuse a number of different drugs."

Source

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Treating Mood Disorders in Drug Abuse Patients Yields Improvement in Both Conditions

By Patrick Zickler, NIDA NOTES Staff Writer

For many drug abuse patients, mood disorders are a constant companion. Among cocaine abusers, for example, depressive disorders are the most commonly diagnosed coexisting, or comorbid, conditions. The relationship between mood disorders and drug abuse in these patients is often complex and interconnected: Drug abuse patients may develop depression as a result of the physical and psychological suffering associated with their drug use, and patients suffering from mood disorders may become drug dependent in attempts to self-medicate. For patients suffering from both drug abuse and mood disorders, the conditions once seemed impossible to untangle, but recent NIDA research suggests that treatment for the mood disorder alone also can have a positive effect on drug abuse treatment.

One NIDA-supported study found that drug use declined among teenage drug dependence patients being treated with a medication for bipolar disorder, which is characterized by alternating periods of depression and mania. In a related study, chronic opiate-dependent adults reported less drug abuse when they were treated with the antidepressant imipramine for comorbid depression.

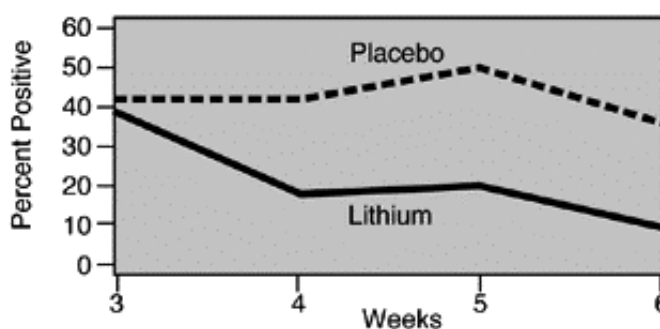
Reducing Substance Dependence in Bipolar Teens

Lithium has proven effective in treating adult bipolar disorder patients and research with adult patients suggests that lithium also may be an effective treatment for comorbid substance dependence. However, no double-blind, placebo-controlled studies have tested the therapy in adolescents. Now, at Washington University in St. Louis, Dr. Barbara Geller and her colleagues have found that, in adolescent patients, lithium treatment for the manic phase of bipolar disorder also reduces drug and alcohol

dependence.

The researchers' double-blind, placebo-controlled study involved 25 teenage patients who had been diagnosed with bipolar disorder and secondary substance abuse disorder involving marijuana, alcohol, inhalants, or multiple drugs. "Most of these kids have had bipolar disorder since the age of 9," Dr. Geller says. "They have been severely ill for a long time, and most are from families with a history of bipolar disorder."

**Percent of Urine Samples Positive for Drugs:
Patients Taking Lithium vs. Patients
Taking a Placebo**



Random weekly urine analysis showed significantly lower drug use among patients who received lithium compared with patients who received a placebo.

More than half of the patients also came from families with a history of substance abuse, sometimes reaching back several generations. All had begun using drugs in the year prior to being enrolled in the study. "Secondary substance dependence disorders are the most common and most severe comorbidity in bipolar patients," Dr. Geller says. "We wanted to get to them within the first year, when they were newly addicted."

All participants in the study received packets of capsules to be taken twice each day during the 6-week study. For half the teenagers, the capsules contained lithium dosages that have proven effective in treating adult bipolar patients. The other patients received placebo only. All participants, who were treated as outpatients, also received weekly therapy sessions. Blood levels of lithium were checked twice each week—once randomly—to make sure the participants were taking the pills. Urine samples were collected twice weekly—once randomly—to monitor drug use.

The percentage of drug-positive urine samples for participants receiving placebo remained essentially unchanged, at roughly 40 percent, throughout the study. But for the group receiving lithium, drug-positive urine samples dropped from 40 percent to approximately 10 percent.

“We tested randomly six times during the study and the urine samples confirmed the patients’ self-reports. There was a significant decrease in drug use,” Dr. Geller says.

In addition, patients in the lithium group showed significantly greater improvement in symptoms of bipolar disorder—such as their ability to function in family, school, and social settings—than did those receiving a placebo.

“Lithium treatment of bipolar disorder in adolescents with secondary substance dependence disorders was an efficacious treatment for both disorders,” Dr. Geller concludes.

Reducing Craving in Methadone Patients

Dr. Edward Nunes and his colleagues at the New York State Psychiatric Institute and Columbia University College of Physicians and Surgeons in New York City found that antidepressants used to treat comorbid depressive disorders in adult methadone treatment patients not only can improve their mood but also reduce their craving for drugs.

“We were able to identify and treat primary or secondary depression in chronically drug-dependent adults,” Dr. Nunes says. “In some respects, treating depression as a separable disorder represents a sea change in the way we look at comorbidity in these patients.”

In Dr. Nunes’ study, patients receiving imipramine to treat depression showed substantial drops in depressive symptoms, and many patients whose depressive symptoms improved also reported decreased craving and use of drugs, including opiates, cocaine, and marijuana.

“There is evidence that treating the depression helps some patients take advantage of therapy and could be successful as one part of treatment,” Dr. Nunes says.

The 12-week study involved 137 patients recruited from 2 community-based methadone maintenance programs. Patients also were diagnosed with primary depression that predated their drug use or secondary depression that emerged or persisted through a period of abstinence or had lasted for at least 3 months during a current period of drug use. Patients were randomly assigned to either imipramine or placebo. Eighty-four patients completed at least 6 weeks of the trial. Fifty-seven percent of patients receiving imipramine were rated as having substantial improvement in both mood and drug use compared with only 7 percent among the patients receiving placebo. Fourteen percent of patients receiving imipramine achieved abstinence, confirmed by urinalysis, for 4 weeks compared with 2 percent of patients who received placebo.

“Imipramine had a very robust and positive effect on mood. This improved mood was associated with less intense and less frequent drug craving and, to a lesser extent, with reduced drug use,” Dr. Nunes says.

Sources

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Matching Drug Abuse Treatment Services to Patient Needs Boosts Outcome Effectiveness

By Neil Swan, *NIDA NOTES* Staff Writer

Matching a drug abuse treatment patient with the right type of treatment program is a much-discussed but elusive goal for drug abuse treatment providers. In the real world, a patient simply may not have the option of switching to another treatment program that might be a better match for his or her needs. For example, a patient's choices may be limited by the insurers, employers, or Government programs that pay for the treatment.

Even within these limitations, however, treatment needs can be evaluated and special services can be targeted to meet patients' specific needs with effective outcome results, NIDA-funded research shows.

Dr. Thomas McLellan and his colleagues at the University of Pennsylvania in Philadelphia first sought to develop and evaluate a clinically practical matching procedure for assigning patients to treatment programs that were deemed most appropriate to the patients' needs. But the investigators could find no evidence of better outcomes for any particular type of patient, regardless of whether

the assigned program was inpatient or outpatient. The researchers also found that insurance coverage requirements made it difficult to place patients in selected treatment programs even when the patients were willing to go to that program.

So the researchers redirected their goal from "matching patients with programs" to "matching patients' problems with targeted therapy services" furnished within the treatment program that was covered. They compared outcomes of patients in matched-services programs to outcomes of patients receiving standard, unmatched services, in four private treatment programs in Philadelphia - two inpatient and two outpatient programs. The 94 adult patients in the study all were employed and were dependent on drugs, alcohol, or both. All treatment costs were covered by employer-provided insurance.

On entering treatment, patients were interviewed using the Addiction Severity Index (ASI), a standard hour-long interview designed to measure severity of problems in

Changes in the Addiction Severity Index Variables				
	Standard Treatment Patients		Match Services Patients	
Problems	On Entering Treatment	6 Months After Discharge	On Entering Treatment	6 Months After Discharge
PROBLEMS NOT TARGETED				
Days of Alcohol Use	12	2	15	1
Days of Alcohol Intoxication	11	2	13	1
Days of Opiate Use	3	1	1	1
Days of Cocaine Use	4	1	5	1
Days of Medical Problems	4	5	3	3
TARGETED PROBLEMS				
Days Worked	16	14	14	17
Employment Income	\$1,318	\$1,072	\$1,042	\$1,435
Days of Family Problems	4	4	3	1
Days of Psychological Problems	10	7	11	4
<i>Variables reflect the 30 days prior to treatment admission and 6-month followup.</i>				

the following areas: medical symptoms, employment and self-support, drug use, alcohol use, legal status, family and social relationships, and psychiatric symptoms.

Randomly selected matched-services patients received focused services in the areas of employment, family relations, or psychiatric problems, depending on their needs. These problem areas were targeted because studies had shown them to be most important in predicting poor treatment outcome. The treatment providers gave these matched patients a minimum of three individual therapy sessions from a psychiatrist, psychologist, or social worker, for each identified problem. For example, matched patients with a psychiatric problem received at least three targeted individual therapy sessions from a psychiatrist or psychologist. Standard patients were also interviewed with the ASI. The information was provided to the treatment programs, and the programs were asked to treat them "in the usual manner."

Both matched- and standard-treatment patients were monitored with weekly phone calls and were evaluated again with the ASI interview 6 months after discharge. The results showed that matched-treatment patients stayed in treatment longer, were more likely to complete treatment, and had better 6-month outcomes than the standard-care patients treated in the same programs. The standard-care group showed significant improvements between admission and 6-month followup in drug use, alcohol use, family relations, and psychiatric problems, but failed to show improvements in medical status and showed significantly worsened status in employment.

The matched group showed statistically significant improvement in all ASI problem areas.

The researchers caution against generalizing their findings to other groups. The study patients were referred by an employee assistance program and thus probably differed from other insured groups in the amount of pressure they were under to enter treatment, as well as in aspects of their backgrounds, the researchers note.

The matching strategy was clinically and administratively practical and attractive to patients, the researchers say. The results indicate that, despite obstacles to matching patients to programs, strategies can be designed to target services effectively within programs.

"In the real world of addiction treatment, providers can find ways to best utilize treatment resources," says Dr. McLellan. "Each patient's unique treatment needs can be identified easily and reliably at the time of treatment admission, and the appropriate services can then be targeted to that patient as part of the overall treatment. It's not very different from what most treatment clinicians describe as individually tailored treatment."

Source

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Men and Women in Drug Abuse Treatment Relapse at Different Rates and for Different Reasons

By Steven Stocker, *NIDA NOTES* Contributing Writer

Recent NIDA-funded studies have found that women in drug abuse treatment relapse less frequently than men do, at least partly because women are more likely to engage in group counseling. Other NIDA-supported researchers have found that cocaine-addicted women and men differ in the factors that cause them to relapse, indicating that males and females might benefit from different relapse prevention strategies.

Likelihood of Relapse

In a study conducted at the University of California, Los Angeles, Dr. Robert Fiorentine and his colleagues have found that women drug abusers are less likely than men drug abusers to relapse after entering treatment because women participate more frequently in group counseling and that this more intensive level of treatment engagement helps them to remain drug-free.

The researchers followed 182 women and 148 men in 26 public outpatient drug abuse treatment programs in Los Angeles County. The programs provided group, individual, and family counseling; educational activities; and referrals to other health and social services. The treatment lasted 6 months.

About half the patients regularly used just one drug—primarily crack cocaine, marijuana, or powder cocaine, and about half used more than one drug. Regular use was defined as three or more times per week. The patients were interviewed while in treatment and approximately 6 months after the first interview.

The scientists found that the women in their sample were less likely than the men to relapse: only 22 percent of the women compared to 32 percent of the men relapsed to drug use in the 6 months between interviews. The researchers considered several theories to account for this finding.

One possibility was that the women used drugs less than the men, so abstaining from drug use was easier for them. However, the study findings showed otherwise. In the year preceding treatment, more women had used crack cocaine than men, and about the same percentages of women and men had used powder cocaine, marijuana, and other drugs. In addition, women used all drugs as frequently as men, except for crack and heroin, which women used more frequently. Finally, about the same percentage of women and men used two or more drugs.

Another possibility the researchers considered was that the women received more social support than the men from a variety of sources, such as families, friends, and coworkers. The investigators found that, although the women were more likely than the men to maintain a social network, they were no more likely than men to receive emotional support for their problems and encouragement to stop using drugs.

What did appear to explain the difference in relapse was the fact that the women were more likely to engage in treatment, particularly group counseling, says Dr. Fiorentine. In his study, the women engaged in an average of 10.9 sessions of group counseling per month compared to 7.9 sessions a month for the men. Research has shown that more intense participation in treatment is associated with lower rates of relapse.

The women did not seem to be attending group counseling sessions more often than men because the sessions were somehow oriented more toward women. The sessions dealt with the problems of both genders more or less equally and were usually attended by both men and women, Dr. Fiorentine says.

The reason that women attended group counseling sessions more than men may stem from women's greater willingness to seek professional help for their health problems, speculates Dr. Fiorentine. "Women appear to be more willing to seek help for their problems, including their substance abuse problems," he says. "Men, on the other hand, are more likely to say, 'I'm OK. I don't need help. I can take care of this. It's just a little problem.'" He recommends that treatment providers discuss with male drug abusers the possibility that their reluctance to seek help may be hampering their recovery.

Even though the women attended more group counseling sessions than men, they did not attend more individual counseling or family counseling sessions than men did. If women are more likely to use services in general, why did they not engage more often in these other types of therapies? The explanation seems to be that these other therapies are not offered as frequently as group counseling in Los Angeles County, primarily because of the county's budget constraints, Dr. Fiorentine suggests. "Individual counseling, for example, is expensive and there are only so many counselors to go around, so treatment programs ration individual counseling," he says.

“Both women and men already may be attending the maximum number of individual counseling sessions they can attend. If patients could attend as many of these sessions as they desired, you might see more women than men in these sessions, just as you see more women than men in group counseling sessions.”

In a related study, Dr. Roger Weiss and his colleagues at McLean Hospital in Belmont, Massachusetts, also found less likelihood of relapse for women than for men among patients who were hospitalized for cocaine addiction. When 74 patients were interviewed 6 months after the hospitalization, 51 percent of the women had remained abstinent compared to 25 percent of the men.

Like Dr. Fiorentine, Dr. Weiss theorizes that the women in his sample were more motivated for therapy than the men were. “Studies have identified barriers to entering drug abuse treatment programs that exist for women but not for men,” says Dr. Weiss. “These include childcare difficulties and the predominance of male patients and staff. There is also more social stigma for women in being labeled an addict. Women who come to these treatment facilities must be willing to overcome these barriers, which could lead to a higher percentage of women who are motivated to change.”

Reasons for Relapse

In addition to identifying gender differences in the likelihood that drug abusers relapse, scientists also have identified gender differences in drug abusers’ experiences before and during relapse. Dr. James McKay and his colleagues at the University of Pennsylvania in Philadelphia found that women in treatment for cocaine addiction were more likely than men to report negative emotions and interpersonal problems before they relapsed. The men, on the other hand, were more likely to report positive experiences prior to relapsing and were more likely to engage in self-justification and rationalizing afterward. They reported, for example, that they felt entitled to use cocaine or that they believed they could control their cocaine use. The women also were much more likely to be impulsive in their return to cocaine use. Fifty-six percent of the women, compared with only 17 percent of the men, reported that they relapsed immediately after the thought of using cocaine occurred to them.

These gender differences in relapse factors suggest that different relapse prevention strategies might be emphasized for women and men, says Dr. McKay. For example, women might benefit more from techniques that enable them to deal more effectively with unpleasant emotions and interpersonal problems. “One strategy is to take action quickly as your mood starts to deteriorate rather than waiting until you are in a really bad mood and then trying to do something about it,” he says. “If it’s a small

problem, planning an enjoyable activity might be all that is needed. If, however, it’s a serious depression, medication or psychotherapy might be necessary.”

In contrast, men might benefit more from strategies that counter their tendency to let down their guard when feeling good, Dr. McKay says. “These strategies are derived from concepts taught in 12-step programs, such as not getting too cocky or confident when your mood improves,” he says. “Patients are told to be on the lookout for warning signs that might be present when they’re feeling good, such as thinking to themselves, ‘I’m feeling great today. I don’t need to go to that meeting. I can go hang out with this friend of mine. I know he uses, but I’m feeling good today, and I’m not vulnerable to using.’”

More Research

Gender differences in drug abuse are of intense interest to NIDA, says Carol Cowell of NIDA’s Division of Clinical and Services Research. “Researchers are finding gender differences across the broad spectrum of drug abuse research—from basic research to studies such as these on treatment and services—and we would like to encourage more study of these differences,” she says. She occasionally suggests that NIDA-funded researchers analyze their data in terms of gender differences. “This sometimes results in a study that increases our knowledge of the role of gender in treatment outcomes,” she says.

“Performing gender analyses is simply a matter of doing good science,” says Dr. Cora Lee Wetherington, NIDA’s women’s health coordinator. When gender differences exist but investigators fail to test for them, flawed conclusions may be drawn, either for males or females or both, she says.

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Drug Addiction Treatment Conference Emphasizes Combining Therapies

By Steven Stocker, *NIDA NOTES* Contributing Writer

Drug addiction can often be treated best through a combination of behavioral and pharmacological treatments and social service interventions, according to speakers at NIDA's National Conference on Drug Addiction Treatment. The conference, held in Washington, D.C., in April, attracted more than 800 drug abuse treatment researchers and service providers, leaders of professional organizations, criminal justice and law enforcement personnel, representatives from State drug abuse agencies, and public policymakers. The conference was presented as part of NIDA's Treatment Initiative, which is designed to improve the quality of the Nation's drug abuse treatment. (See "NIDA Launches Drug Abuse Treatment Initiative," *NIDA NOTES*, Vol. 12, No. 4).

Research is showing that drug addiction therapy that combines different approaches is often more effective than therapy that uses only one approach, said NIDA Director Dr. Alan I. Leshner. "When all is said and done, the ultimate cure for drug addiction will probably involve a combination of biological and behavioral treatments and social services," he said.



At the conference, Dr. Mary Jeanne Kreek of Rockefeller University describes the health benefits of methadone treatment combined with behavioral treatments.

This approach of treating drug addiction by combining biological and behavioral therapies stems in part from studies showing that addiction is both a biological and a behavioral disorder, Dr. Leshner said. "What science has taught us is that drug addiction is a result of an interaction between an individual's biological vulnerability plus his or her experiences plus environmental factors plus, of course, drugs. The final result is a changed brain," he said. Viewing drug addiction as exclusively biological or behavioral is too limiting, he cautioned. "Let us not pit biology against behavior. These are not opposing viewpoints."

Combining medications with behavioral treatments can have an additive effect on therapy because the different treatments work on different aspects of addiction, said Dr. Bruce Rounsaville of Yale University in New Haven, Connecticut. Medications, such as methadone or medications that treat psychiatric disorders, can increase the chances that patients will stay in treatment. Psychotherapy can then help motivate patients to abstain from drugs and help them develop healthier lifestyles, said Dr. Rounsaville. Several speakers examined behavioral therapies that are proving effective in treating drug addiction.

Dr. Kathleen Carroll of Yale University School of Medicine described cognitive-behavioral therapy (CBT), a comparatively brief intervention that helps cocaine-dependent individuals become abstinent from cocaine and other substances. In CBT, patients learn to recognize and avoid the situations in which they are most likely to use cocaine. They also learn how to cope with their urges to use cocaine and to deal with their psychological, occupational, and other problems. "Drug use requires skills involving getting the money to buy drugs, getting the drugs, and other activities," said Dr. Carroll. "In CBT, the patient learns that he or she has the capacity to learn skills that are healthier and more productive," she said.

Another effective behavioral approach involves rewarding patients for staying abstinent, according to Dr. Maxine Stitzer of Johns Hopkins University in Baltimore. For example, patients can be given vouchers as a reward for drug-free urines. The vouchers can be exchanged for healthful goods or services valued by the patients.

In family therapy for drug addiction, the therapist suggests ways that family members can help their addicted relatives stop abusing drugs, said Dr. José Szapocznik of the University of Miami School of Medicine in Miami, Florida. In one situation, for example, a mother ordinarily may allow her adult drug-abusing daughter to stay with her for several days in between drug binges, despite her misgivings about the daughter's drug abuse. In family therapy, the therapist might encourage the mother to set limits for her daughter, such as allowing her to stay only if she agrees to remain abstinent. In addition to helping an addict, family therapy also has the potential for reaching other members of the family who may themselves have problems with drug abuse, said Dr. Szapocznik.



At NIDA's treatment conference, Dr. Kathleen Carroll of Yale University describes how cognitive behavioral therapy can help patients learn to avoid situations in which they are likely to use cocaine.

Dr. Herbert Kleber of Columbia University in New York City reported on detoxification techniques that help opiate addicts cope with withdrawal symptoms when they stop using opiates. Newer techniques include the use of a combination of the opiate treatment medications buprenorphine, clonidine, and naltrexone and the use of anesthesia or heavy sedation. Detoxification is only the first step in treating opiate addicts, Dr. Kleber stressed. "You should measure success not only by the level of comfort during withdrawal but also by how many patients go on for further therapy," he said.

Other speakers discussed the challenges of providing drug abuse treatment for special populations. For example, individuals with both severe mental disorders, such as schizophrenia, and drug abuse disorders should be treated for both conditions concurrently, said Dr. Robert Drake of Dartmouth Medical School in Hanover, New Hampshire. This is best accomplished by multidisciplinary case management teams that might include a psychiatrist, a mental health case manager, a substance abuse specialist, and a vocational specialist who can address the patient's needs in an integrated fashion.

This approach yields a number of benefits, including fewer relapses and hospitalizations and a higher functional status, said Dr. Drake.

Many drug-abusing adolescents also have a mental disorder, such as conduct disorder or depression, said Dr. Paula Riggs of the University of Colorado Health Sciences Center in Denver. These disorders contribute to the severity of the drug abuse disorder and should be treated concurrently, she said.

Drug abuse treatment can have health benefits in addition to reducing drug use, according to several speakers. Dr. David Metzger of the University of Pennsylvania in Philadelphia described numerous studies demonstrating that drug abuse treatment reduces the rates of HIV infection, by reducing both syringe sharing and risky sexual behaviors. Dr. Mary Jeanne Kreek of Rockefeller University in New York City presented data showing that, among injection drug users in New York City, methadone treatment, when combined with appropriate behavioral treatment, is reducing rates of both HIV infection and hepatitis B and, to a lesser extent, hepatitis C. Methadone treatment can also improve the health of addicts by normalizing immune function and the levels of stress and sex hormones, all of which are altered by drug abuse, Dr. Kreek said.

Thirteen million people in the United States currently abuse drugs, and 4 million are compulsive drug abusers, said General Barry McCaffrey, director of the Office of National Drug Control Policy, in the keynote address. The goal is to reduce the percentage of the U.S. population that is abusing drugs to under 3 percent by 2007, he announced. **NN**

Study Sheds New Light on the State of Drug Abuse Treatment Nationwide

By Michael D. Mueller and June R. Wyman, *NIDA NOTES* Staff Writers

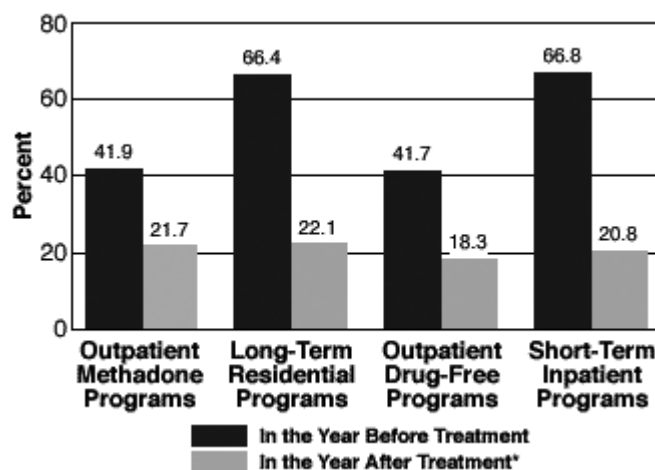
The four most common forms of drug abuse treatment are all effective in reducing drug use. That is the major finding from a NIDA-sponsored nationwide study of drug abuse treatment outcomes. The Drug Abuse Treatment Outcome Study (DATOS) tracked 10,010 drug abusers in nearly 100 treatment programs in 11 cities who entered treatment between 1991 and 1993.

"DATOS is the largest study of drug abuse treatment outcomes since the early 1980s and the most important in the last 10 years in terms of telling us how treatment programs are doing," says Dr. Bennett Fletcher, chief of NIDA's Services Research Branch.

DATOS investigators measured treatment outcomes using a random sample of approximately 3,000 patients. The researchers compared patients weekly and daily drug use for the 12 months before they entered treatment with their weekly and daily drug use 12 months after they stopped treatment. Patients in outpatient methadone treatment who were still in treatment were interviewed approximately 24 months after admission. Other outcomes that the researchers measured included:

- whether patients reported fewer illegal acts, including assault, robbery, burglary, larceny, forgery, and fencing stolen property;
- whether patients were working full time, defined as at least 35 hours per week; and
- whether patients reported fewer attempts or thoughts of suicide, which was used as a marker for depression. The researchers chose that marker because several previous studies had established its validity as an indicator of depression.

Percentage of Patients Reporting Weekly or More Frequent Cocaine Use Before and After Treatment



* Outpatient methadone patients still in treatment were interviewed approximately 24 months after admission.

In all four types of treatment programs that the Drug Abuse Treatment Outcome Study examined, the percentage of patients reporting frequent use of cocaine dropped dramatically after treatment.

The four types of programs with the number of programs that DATOS studied in parentheses were outpatient methadone (29), outpatient drug-free (32), long-term residential (21), and short-term inpatient (14). (For descriptions of the program types, see the textbox on next page.) Three of the four types were also studied in DATOS's two predecessors: the Drug Abuse Reporting Program (DARP), which included admissions to treatment from 1969 to 1973, and the Treatment Outcome Prospective Study (TOPS), which covered admissions from 1979

to 1981. The short-term inpatient treatment programs, originally developed to treat alcohol abuse but admitting increasing numbers of cocaine abusers during the 1990s, were studied in DATOS but not in the two earlier projects.

Highlights From the Study

For the four treatment types, DATOS investigators found reductions almost without exception in the use of all drugs including cocaine, heroin, and marijuana after treatment. (See "Percentages of Patients Reporting Weekly or More Frequent Substance Use Before and After Treatment" on next page.) Likewise, after treatment a smaller percentage of patients reported committing illegal acts, working less than full time, and thinking about or attempting suicide. (See "Percentage of Patients Reporting These Behaviors Before and After Treatment" on last page of article.) The data also revealed that:

- Except in outpatient methadone programs, cocaine was the primary drug of abuse, with alcohol running a close second. Cocaine abuse was common even in

Four Common Types of Drug Abuse Treatment

Investigators with the Drug Abuse Treatment Outcome Study (DATOS) studied patients in the four most common kinds of treatment programs:

- **Outpatient methadone programs** administer the medication methadone to reduce cravings for heroin and block its effects. Counseling, vocational skills development, and case management to help patients access support services are used to gradually stabilize the patients functioning. Some patients stay on methadone for long periods, while others move from methadone to abstinence.
- **Long-term residential programs** offer around-the-clock, drug-free treatment in a residential community of counselors and fellow recovering addicts. Patients generally stay in these programs several months or

up to a year or more. Some of these programs are referred to as therapeutic communities.

- **Outpatient drug-free programs** use a wide range of approaches including problem-solving groups, specialized therapies such as insight-oriented psychotherapy, cognitive-behavioral therapy, and 12-step programs. As with long-term residential treatment programs, patients may stay in these programs for months or longer.
- **Short-term inpatient programs** keep patients up to 30 days. Most of these programs focus on medical stabilization, abstinence, and lifestyle changes. Staff members are primarily medical professionals and trained counselors. Once primarily for alcohol abuse treatment, these programs expanded into drug abuse treatment in the 1980s.

outpatient methadone treatment programs for heroin addicts. About 42 percent of patients who entered methadone treatment programs also abused cocaine.

- Heroin use had decreased since the 1979 to 1981 period that TOPS studied. Large declines in the abuse of depressants such as barbiturates and tranquilizers had also occurred since TOPS.
- Short-term inpatient treatment programs yielded significant declines in drug use, even though patients stayed in these programs no more than 30 days. "This is one of our most surprising findings," Dr. Fletcher says. "This treatment mode had a high percentage of patients reporting daily or weekly use of cocaine in the year before treatment and a sharp decline in weekly and daily use after treatment." The percentage of patients reporting illegal acts and thoughts of suicide also declined significantly after treatment in these programs. The researchers are exploring whether continuing involvement in outpatient services and mutual help groups may have contributed to these positive outcomes.
- In every city studied in DATOS, support services such as medical, legal, financial, psychological, employment, and family services had declined dramatically since TOPS, while the need for those services had increased. (See "DATOS Documents Dramatic

Decline in Drug Abuse Treatment Services," *NIDA NOTES*, Vol. 12, No. 5).

- Patients surveyed by DATOS reported that it took them about 7 years after they first used their primary drug to enter treatment. (See "Treatment Histories: The Long View of Addiction," *NIDA NOTES*, Vol. 12, No. 5).

New Demographics

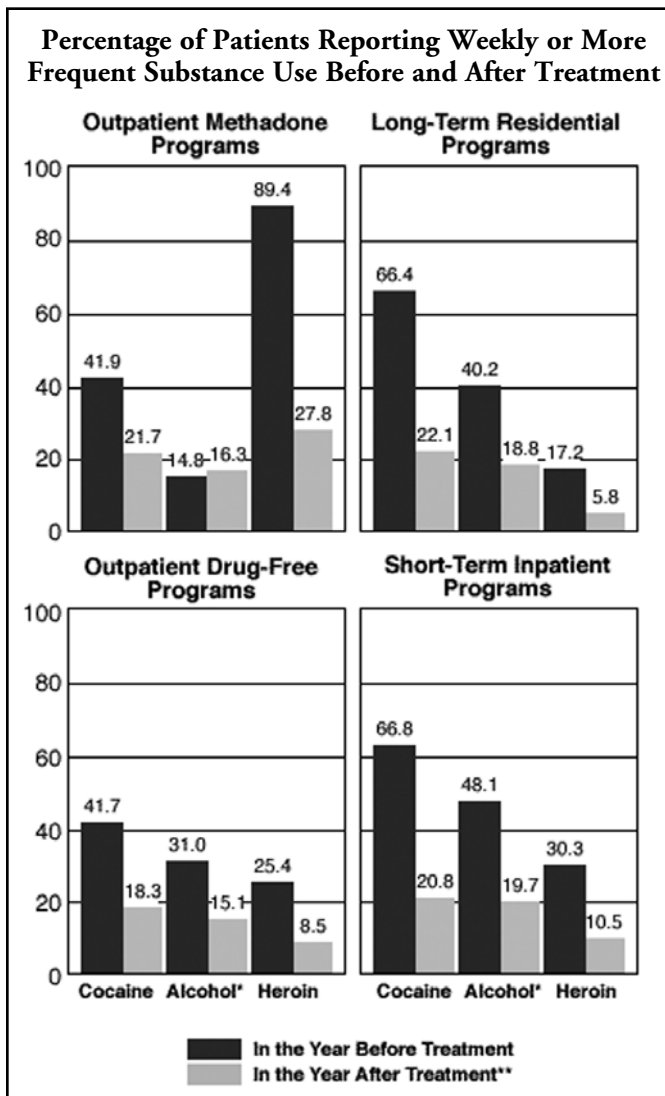
Demographic characteristics of patients studied in DATOS had changed since the earlier study. For example, DATOS patients were older and had more years of schooling than TOPS patients, and a greater percentage of them were women.

In DATOS, 39 percent of patients admitted to outpatient methadone programs were women compared to approximately 31 percent in TOPS. Women made up approximately 33 percent of the patients admitted to long-term residential programs, as opposed to 22 percent for TOPS. Outpatient drug-free programs saw little change from TOPS to DATOS, with women accounting for approximately 33 percent of patients in these programs in both studies. In DATOS, about 37 percent of patients admitted to short-term inpatient programs, which were not included in TOPS, were women. The researchers are conducting additional analyses to further explore the characteristics and outcomes for women in DATOS.

The Drug Abuse Treatment Outcome Study found reductions in the use of all drugs including cocaine, heroin, and marijuana after treatment.

Substance Abuse and Psychological Disorders

DATOS researchers looked at co-occurring psychological disorders and dependencies in 7,402 patients in the DATOS programs who were diagnosed as substance dependent. They found that 32.1 percent of those patients were dependent on cocaine alone. Of that 32.1 percent,



* Weekly or more frequent use with 5 or more drinks at a sitting.

** Outpatient methadone patients still in treatment were interviewed approximately 24 months after admission.

Patients in programs surveyed for DATOS showed a marked reduction in drug use after treatment regardless of the type of treatment program in which they participated. DATOS analyses focused on marijuana use instead of heroin use among patients in short-term inpatient programs and outpatient drug-free programs because the number of patients using heroin in those programs was too small to allow statistical comparisons.

59.1 percent were male. Another 26.3 percent of the patients were dependent on both cocaine and alcohol, and, of those, 69.8 percent were male. In addition, 10.6 percent of the patients were dependent on heroin alone, and 64.2 percent of those were male.

The prevalence of co-occurring psychological disorders among the group was high, especially for antisocial personality disorder (APD) and major depression. APD was characterized as a pattern of disregard for the rights of

others, irresponsibility, and lack of remorse. Major depression was characterized as either a depressed mood or a loss of interest or pleasure for 2 weeks or more.

The prevalence of those two disorders differed widely among men and women. Approximately 40 percent of the group was diagnosed with APD, and males were twice as likely as females to be diagnosed with the disorder. While 12 percent of the group had experienced a major depression, female patients were twice as likely as male patients to have done so.

When the researchers looked at retention rates, they found big differences within each of the four treatment types and among individual programs.

Keeping Patients in Treatment

When the researchers looked at retention rates, they found big differences within each of the four treatment types and among individual programs. “We found a lot of diversity in how well they’re doing at keeping patients in treatment, and we wanted to know why,” says Dr. Dwayne Simpson of Texas Christian University in Fort Worth.

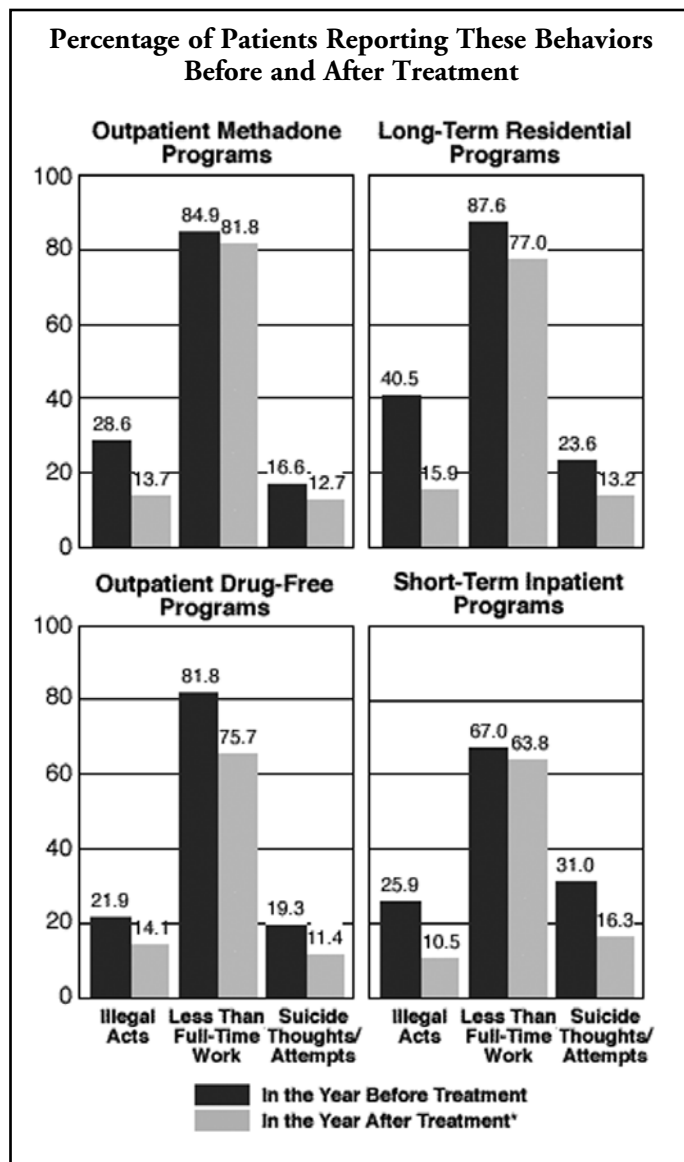
The investigators found that programs with low retention rates tended to have patients with the most problems, particularly antisocial personality disorder, cocaine addiction, or alcohol dependence. In addition, heroin abusers who also abused crack cocaine but not powder cocaine had significantly lower retention rates than other heroin abusers did. “These programs are dealing with some tough people. Programs with the highest concentration of these problem patients naturally tend to have low retention,” Dr. Simpson says.

What makes patients stay in treatment? The researchers found that the major predictors were:

- high motivation;
- legal pressure to stay in treatment;
- no prior trouble with the law;
- getting psychological counseling while in treatment; and
- lack of other psychological problems, especially antisocial personality disorder.

Lessons From DATOS

What were the overall conclusions? “Clearly there were significant changes from before to after treatment in each of the four modalities,” says Dr. Fletcher. That finding



* Outpatient methadone patients still in treatment were interviewed approximately 24 months after admission.

The DATOS data showed reductions after treatment in illegal acts, which included assault, robbery, burglary, larceny, forgery, and fencing; less than full-time employment; and suicidal thoughts and suicide attempts, indicators of depression.

raises some interesting questions, he adds. "For example, retention has been our most powerful and consistent predictor of treatment outcomes - yet even people in short-

term inpatient treatment for 30 days or less improved significantly." Although DATOS replicated the finding from DARP and TOPS that time in treatment is important, the relationship to retention of other factors such as motivation, psychiatric comorbidity, and treatment process needs to be studied more, he says.

One would also expect worse outcomes from DATOS compared to TOPS because of the steady decline in availability of support services, says Dr. Fletcher. A possible explanation for the better DATOS outcomes is that although support services have decreased, core treatment services have improved. "Core services - basic treatment techniques such as drug abuse counseling, mutual-help groups, and patient participation in devising treatment plans may have improved over the past 10 years. What we're seeing may be a result of this improvement, even though availability and use of noncore support services have declined," Dr. Fletcher says.

The study's encouraging results verify the effectiveness of drug abuse treatment no matter what its form, says NIDA Director Dr. Alan I. Leshner. "The service system has changed dramatically over the last two decades. This study gives us a unique opportunity to understand the effect of those changes and to have an impact on the way treatment is delivered," Dr. Leshner says.

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Peer Community Helps Homeless Drug Abusers With Mental Illnesses Reduce Drug Use

By Neil Swan, NIDA NOTES Staff Writer

"I made good friends here. I call them family Even the staff, they are my family. They gave me suggestions, ideas, looking to my future. They helped me. . . . I had 2 years of college, but I didn't get anything out of it. I was using [crack]. . . . I see myself with a future now. . . . Now I want to work for my money. I plan to get my children back, and I am seeking housing for me and my children."

- Sarah, a graduate of a program in New York City for homeless, mentally ill substance abusers

Researchers at the Center for Therapeutic Community Research (CTCR) in New York City, one of NIDA's major multidisciplinary research centers, are studying a treatment program they devised to meet the complex psychiatric and substance abuse needs of homeless substance abusers who are also mentally ill. They have designed a "modified therapeutic community (TC)" that provides 24-hour-a-day supervised residential treatment for 12 months or more followed by less intense aftercare in which patients live alone or together in apartments and hold down jobs.

Patients are recruited into the program by counselors at New York City homeless shelters and psychiatric facilities. Staff members, some of them former homeless substance abusers themselves, help make the program attractive to the homeless. The NIDA-funded treatment research was conducted by the Center at the National Development and Research Institutes. Led by CTCR director Dr. George De Leon, the research has shown that the modified TC program can be effective in treating this elusive population that has "fallen through the cracks" in traditional treatment approaches. Patients substantially reduce drug use and criminal behavior following treatment and also find and keep jobs more frequently than before treatment.

The original TC approach was developed to treat serious substance abusers in a residential program by changing their behavior and thinking. Support of the treatment

This program for homeless, mentally ill substance abusers can be effective in treating an elusive population that has "fallen through the cracks" in traditional treatment approaches.

program members—peers and counselors—is a key ingredient of TCs, which have been enhanced over the years with additional services for vocational, medical, family, and other needs. Today's TC has more participation from mental health, medical, and education professionals who

serve along with TC paraprofessionals who are trained recovered addicts.

The TC approach, according to Dr. De Leon and his colleagues, views substance abuse as a disorder of the whole person. Thus the approach provides a combination of social and psychological therapy that fosters change in patients' behavior, attitudes, feelings, and values. Individuals are motivated to change through their interaction with others, including their peers from the streets. The New York City research is built on a concept of "community as method," which uses the treatment community itself and its activities, relationships, and expectations to enable patients to learn about and change themselves.

Dr. Stanley Sacks, CTCR's deputy director, explains that the resident community, which usually consists of 12 to 20 patients, provides a structured daily regimen with morning and evening community meetings, seminars, classes, conflict-resolution therapy sessions, and a peer work structure in which community members maintain the facility and prepare their meals. The residents' progress toward reentry into society by moving first through a transitional program in which they share apartments with other patients. Mutual support and community ties are continued while patients advance toward entering the job market. Some are employed in clerical or maintenance positions; others eventually become peer counselors in similar recovery programs. After 6 to 12 months of transitional apartment living—18 to 24 months after entering the residential program—patients advance to independent living while maintaining kinship ties with peers and holding jobs.

The fundamental needs of the patients were extensive, combining psychiatric, substance abuse, medical, and social problems that were acute and intricately intertwined.

The CTCR study profiled 342 homeless patients as they entered the modified TC program. Interviews by CTCR researchers showed that the fundamental needs of the patients were extensive, combining psychiatric, substance abuse, medical, and social problems that were acute and intricately intertwined. The patients interviewed were three-quarters male and 70 percent African-American, with a median age of 35. The researchers found that 99 percent reported illegal drug use some time in their lives; 24 percent reported injecting drugs. Half reported crack or cocaine as their primary drug of abuse; 22 percent cited alcohol and 16 percent identified marijuana as their secondary substance of abuse. Some 84 percent of the patients had not had a job in the past year. Four in 10 said they had had difficulty throughout their lives in making and keeping friends. Virtually all, 99 percent, of the patients reported past criminal activity, and 81 percent said they had broken the law in the past year. Three-quarters of the patients said they had been tested for infection with HIV, the AIDS virus, and 10 percent reported positive HIV test results.

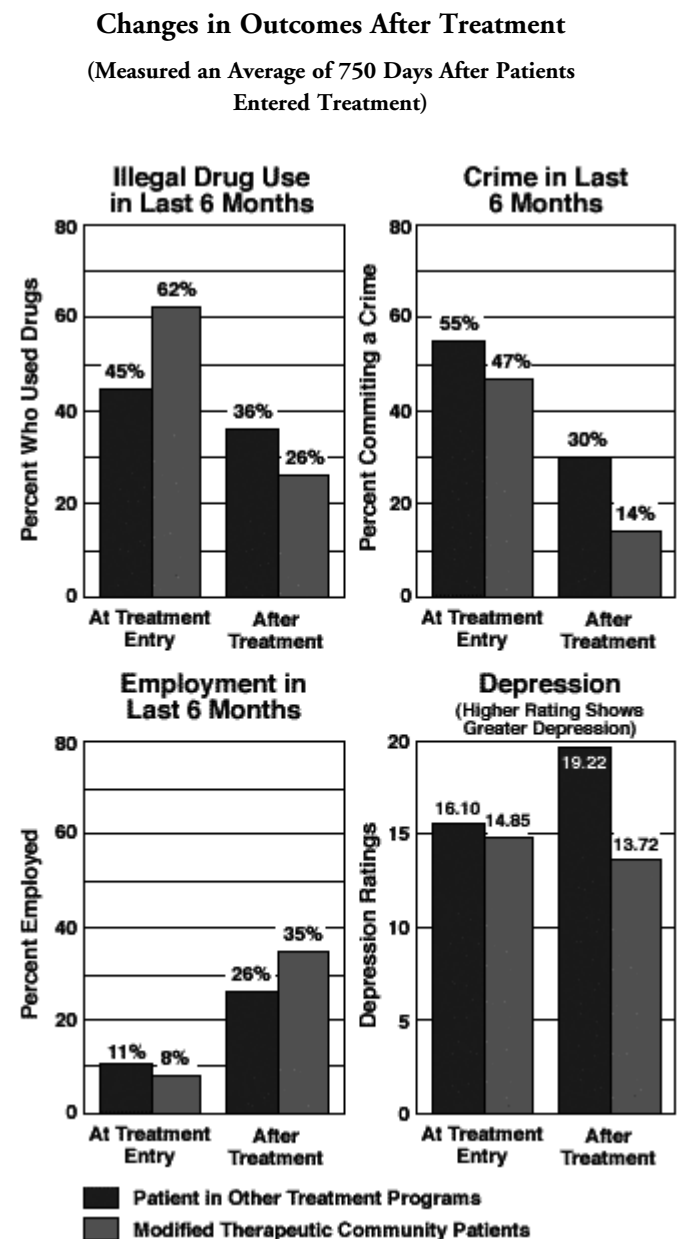
Using a standardized diagnostic test, the researchers also found that 60 percent of their patients had one or more serious mental illnesses—38 percent were diagnosed with major depression, 34 percent with schizophrenia, and 13 percent with mania. When other mental disorders such as posttraumatic stress disorder and phobia were included, 82 percent of the patients had diagnoses of serious mental illness.

The modified TC targets treatment to meet these multi-dimensional needs. Compared to standard TC programs, treatment interventions are more individualized, more flexible, and less intense, explains Dr. Sacks. However, the program remains grounded in peer interactions and the “community as method” concept to foster change, he says.

Even in the face of the homeless patients’ severe and accumulated problems, the modifications to the TC model are proving effective, initial treatment outcome data indicate. Patients in modified TCs had more successful outcomes at followup, an average of 750 days after entering treatment, than did other New York patients with similar diagnoses who were enrolled in more conventional treatment programs. Those in modified TC treatment reported less illegal drug use and less criminal activity and showed

greater improvement on tests to evaluate depression compared with the conventional treatment patients. In addition, those in modified TC showed important gains in employment levels compared with their pretreatment levels (see “Changes in Outcomes After Treatment,” at bottom of page).

Aftercare is critical for these patients as they progress toward independent living, says Dr. De Leon. Mental



Homeless mentally ill patients in a modified therapeutic community in New York City who were treated for both substance abuse and psychiatric problems had more successful outcomes after treatment than did patients with similar disorders in other treatment programs.

health and medical needs are the most pressing, he adds. Patients who enter treatment with a long history of severe drug abuse—10 years or more— and psychiatric problems require more time than do others in the program, he says. But it may be possible to shorten the time in the residential setting with improved aftercare services, he adds.

Currently, NIDA is supporting a CTCR study to examine the cost-effectiveness of the modified TC program. This study is evaluating program costs against benefits to society measured in taxpayer savings through reduced crime and social services expenditures and increased tax revenues as patients become productive wage-earners. Also with NIDA funding, CTCR is evaluating a modified TC for mentally ill substance abusers in the San Carlos Correctional Facility in Pueblo, Colorado.

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Access to Housing and Job Training Helps Recovering Homeless People Stay Drug Free

By Neil Swan, NIDA NOTES Staff Writer

"I came to the city, and my first day here I spent all my money—\$800—on drugs. For the first time in my life I was homeless, and it set into me that I was addicted. . . . I entered treatment, and I think that without drug screening early on, I would never have stayed clean. Housing was important, too. In a shelter or on the streets, being around using people makes it almost impossible to recover. . . . I'm clean today, two years down the road. I work in construction; I made \$40,000 last year. I'm making restitution for my child support. I fly my son down for visits during the summers."

—Mr. C., who successfully completed a treatment program in Birmingham, Alabama with access to housing and work therapy

Therapy targeting homeless crack and alcohol abusers reduces substance abuse more if it offers patients housing and jobs, NIDA-funded research has shown. A key component is a requirement that participants stay drug free to remain in the housing and enter work therapy, according to the study's researchers at the University of Alabama at Birmingham.

This therapeutic approach, in which rules and consequences are applied to help people change their behavior, is called contingency management. In the Birmingham program, access to housing and employment is contingent on following the rules, which homeless participants soon learn: stay clean of drugs and alcohol, and you can live in a furnished apartment and enter work therapy. Test positive for drugs or alcohol and you go back into a shelter and lose your job until you are drug free.

The approach works. The Birmingham researchers have demonstrated that participants in the contingency management program remained abstinent from drugs substantially longer than patients who did not receive contingency-based housing and work therapy. "The contingencies for reinforcements of housing and a job are powerful motivators," says Dr. Jesse B. Milby, principal investigator for the project.

Program participants were either homeless or at risk of becoming so. Three-quarters of the patients were male, and 83 percent were African American. Average age was 38 years; average time spent in school was 12.5 years.



Patients in the Birmingham, Alabama treatment program who participate in the work therapy program develop a sense of pride and kinship while learning job skills such as carpentry and painting.

Some 79 percent met criteria for one or more mental disorders—56 percent for mood disorders, 39 percent for anxiety disorders, 6 percent for adjustment disorders, 4 percent for psychotic or organic mental disorders, and 4 percent for other mental disorders. The drug that participants said they used most frequently was cocaine followed by alcohol then marijuana.

In the study, participants were placed for 2 months either in existing local substance abuse treatment programs or an intensive day treatment program that included contingency management. The conventional treatment program

consisted of weekly, 12-step-oriented group meetings and individual counseling sessions.

The intensive day treatment required program attendance for 5 1/2 hours every weekday, including group and individual counseling sessions and participant involvement in goal-setting exercises. Intensive day treatment patients also received transportation, lunch, and individual counseling. Patients who completed day treatment were then eligible for the contingency management component—housing and 4 months of work therapy refurbishing abandoned or dilapidated houses as long as they stayed drug-free. The renovated dwellings became housing for participants who met contingency requirements. So far, patient-workers have renovated six houses and have worked on four small apartment buildings now used as drug-free housing.

In the work program, patients learned job skills like carpentry and painting. They worked for "Bad Boy Builders," operated by a Birmingham contractor, and received minimum wages, which they used to pay modest rent for their own housing in dwellings that were previously refurbished by other program enrollees. The con-

tractor provided tools, materials, insurance, and on-the-job training. Job references were provided for successful patients seeking to move on to other jobs.

Patients moved into the housing after four successive "clean" urine tests. Those who tested positive for drug use were immediately evicted from their apartments and taken to a local shelter to stay during the eviction. Following two successive clean drug tests, these participants were readmitted to their apartments. Most wanted to move back, and most qualified with clean tests, Dr. Milby says. After completion of the 4-month work therapy, treatment graduates were permitted to remain in the program-provided housing. Some program graduates continue to live in this housing, paying rent.

In the work therapy phase, the program seeks to establish a sense of pride, kinship, and unity among patients. One way the program builds this sense of community is by membership in Club Birmingham. The club holds social activities and distributes identification cards and tee shirts with the club logo.

"We want to provide models of social and recreational activities that are not related to substance abuse," says Dr. Milby. "When they have been homeless and using cocaine and alcohol for a long time, they forget that there are other ways to have fun. We give them a chance to enjoy themselves in drug-free settings like cookouts and fishing parties."

Investigators found that participants in treatment with contingencies were more likely than those in conventional treatment to test clean of drugs, move into stable housing, and be employed regularly following treatment. Those receiving the 4 months of contingency management had 18 percent fewer positive cocaine tests than did conventional care patients after 6 months. That study demonstrated that a multicomponent treatment that addresses homelessness, employment problems, and substance abuse may be the key to successful therapy, Dr. Milby says. However, he notes that participants in the day treatment group spent four times longer in counseling sessions, which is an important variable in addition to contingencies. "We questioned whether the intensive day treatment with contingencies was necessary or whether intensive day treatment alone was sufficient for best results."

A second study was designed to answer this question. In this study, currently under way, all participants are exposed to the intensive day treatment, but only half of

Patients in the study who tested positive for drug use were immediately evicted from the program housing and taken to a local shelter to stay during the eviction. Following two successive clean drug tests, they were readmitted.

the participants receive the abstinence-contingent housing and work therapy. A vocational counselor assists participants in developing job goals. Also, participants are allowed to enter program-provided housing as soon as they are drug-free for four successive tests. As a result, most participants move into the housing during day treatment. Once they complete day treatment, they move into work therapy and begin paying for housing. To help avoid relapse, aftercare therapy follows day treatment.

In this second study, several refinements have been made to the treatment regimen. Each week, patients define specific goals on issues such as addiction, housing, jobs, legal problems, psychiatric concerns, and family relations. "Patients review their own performance in meeting goals, and they are rated aloud by their peers and counselors," says Dr. Cecelia Lee McNamara, project coordinator. "They build self-esteem with a record of accomplishments on their goal sheets."

Following the 4 months of work therapy, clients in day treatment with the contingency management component were drug free an average of twice as many weeks as participants who received only day treatment. The two groups showed equally improved outcomes for days of homelessness and days of employment.

From the second study, it appears that the abstinence contingency works most powerfully on substance abuse, says Dr. Milby. This study also shows that contingency management with day treatment may also reduce the risk of transmission of HIV, the virus that causes AIDS, according to Dr. Joseph Schumacher, another investigator.

Because of the increased costs of providing contingency management, Dr. Milby and his team next plan to study the cost-effectiveness of the enhanced day treatment when used in combination with contingency management.

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